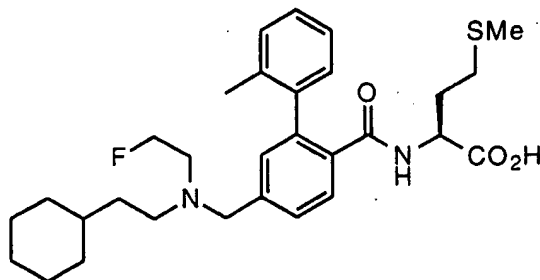


MS m/z 385 ( $M^+ - 1$ , 100).

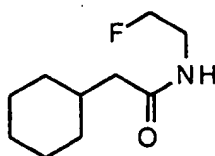
11975



Example 1094

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

11980



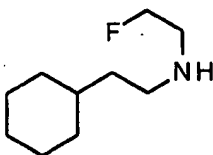
Example 1094A

N-(2-Fluoroethyl)-2-cyclohexylacetamide

11985

Following the procedure of example 1178E, 2-fluoroethylamine•HCl (1.00 g, 10.00 mmol) provided 1.58 g (84%) of the title compound.

MS (DCI,  $\text{NH}_3$ ): 188 ( $\text{MH}^+$ ).



11990

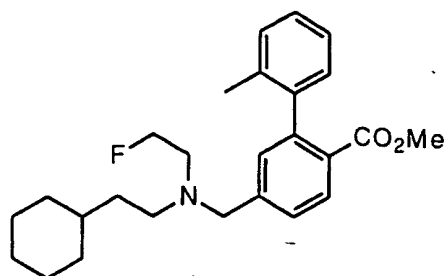
Example 1094B

N-(2-Fluoroethyl)-N-2-cyclohexylethylamine

Following the procedure of example 1178F, example 1094A (1.54 g, 8.2 mmol) provided 1.30 g (92%) of the title compound.

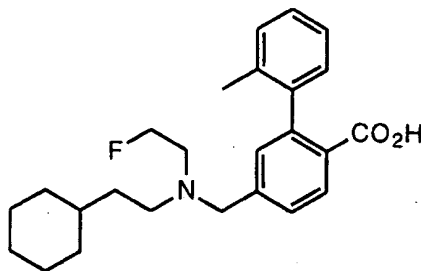
MS (DCI,  $\text{NH}_3$ ): 172 ( $\text{MH}^+$ ).

11995

Example 1094C

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

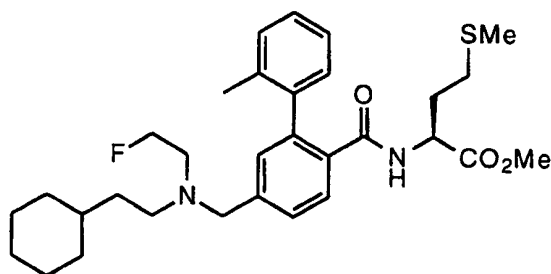
12000 Following the procedure of example 1178G and substituting potassium phosphate for diisopropylethylamine, and heating at 60°C for 60 hours, example 1094B (188 mg, 1.10 mmol) provided 288 mg (70%) of the title compound.  
MS (ESI +): 410 (M + NH<sub>4</sub><sup>+</sup> - F<sup>-</sup>).

Example 1094D

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoic acid

12005 Following the procedure of example 1178H, example 1094C (0.28 g, 0.68 mmol) provided 0.25 g (93%) of the title compound.

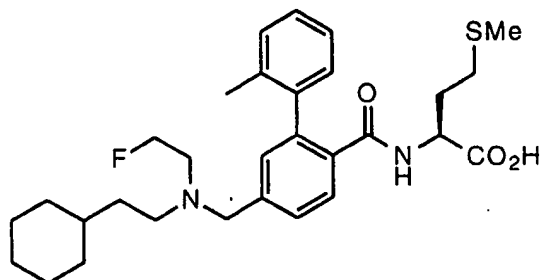
12010 MS (DCI, NH<sub>3</sub>): 398 (MH<sup>+</sup>).

Example 1094E

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

12015

Following the procedure of example 1178 I, example 1094D (245 mg, 0.62 mmol) provided 257 mg (77%) of the title compound. MS: (ESI+): 541 (MH)<sup>+</sup>; (ESI-); 539 (M-H).



12020

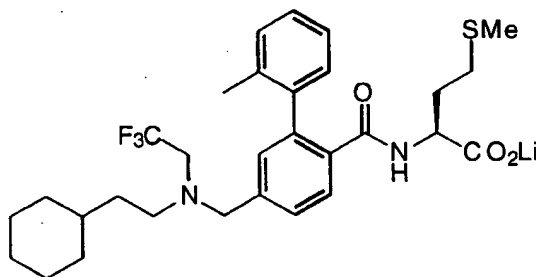
Example 1094F

N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1104D, example 1094E (250 mg, 0.46 mmol) provided 240 mg of the title compound.

12025

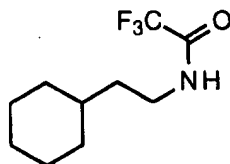
<sup>1</sup>H NMR (δ, CDCl<sub>3</sub>): 7.75 (2H), 7.0-7.4 (4H), 6.4 (1H), 3.8-4.6 (9H), 2.9-3.3 (4H), 0.8-2.3 (21H). MS: (ESI+): 527 (MH)<sup>+</sup>; (ESI-); 525 (M-H). Calc'd for C<sub>30</sub>H<sub>41</sub>FN<sub>2</sub>O<sub>3</sub>S•0.90H<sub>2</sub>O: C 66.12 H 7.92 N 5.14; Found: C 66.13 H 7.77 N 4.86.



12030

Example 1103

N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt



12035

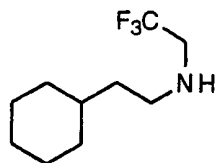
Example 1103A

N-trifluoroacetyl-2-cyclohexylethyl amide

Cyclohexylethylamine (1.27 g, 10 mmol) was dissolved in 10 mL of methylene chloride and pyridine (1.8 mL, 15.0 mol) was added and the mixture cooled to -10° C in an

12040 ice/acetone bath. The solution was treated with trifluoroacetic anhydride (1.7 mL, 12.0 mmol) in 5 mL of methylene chloride dropwise. After stirring for 2 hours at 0°C the mixture was diluted with 100 mL of ether and extracted with water, 1M aqueous phosphoric acid and saturated aqueous sodium bicarbonate, dried, filtered and concentrated to give a white solid (2.07g, 92%).

12045 MS (DCI, NH<sub>3</sub>): 241 (M+NH<sub>4</sub>)<sup>+</sup>.



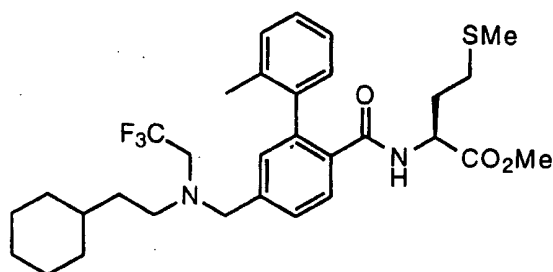
Example 1103B

N-2-trifluoroethyl-2-cyclohexylethyl amine

12050 A solution of lithium aluminum hydride (9 mL of a 1M solution in THF, 9 mmol) was added to a solution of example 1103A (0.67 g, 3.0 mmol) and the mixture was heated to reflux for 2 hours and then cooled to room temperature. The reaction was quenched by the same procedure as example 1178F to provide 0.58 g (92%) of the title compound.

MS (DCI, NH<sub>3</sub>): 228 (M+NH<sub>4</sub>)<sup>+</sup>.

12055



Example 1103C

N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

12060 A solution of example 1103B (210 mg, 1.0 mmol) and the aldehyde from example 403G (192 mg, 0.5 mmol) in 3 mL of 1,2 dichloroethane was treated with acetic acid (0.14 mL, 2.5 mmol) and the mixture stirred for 10 minutes. The mixture was treated with sodium triacetoxyborohydride (213 mg, 1.0 mmol) and the mixture stirred overnight. The work-up was the same as that of example 1134E. The crude product was purified by chromatography on silica gel (20 g, 20% ethyl acetate/hexanes) to provide 96 mg (33%) of the title compound.

12065 <sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 7.91, dd, 1H; 7.42, dd, 1H; 7.18 - 7.36, m, 4H; 7.15, bs, 1H; 5.88, bd, 1H; 4.63, m, 1H; 3.83, s, 2H; 3.65, s, 3H; 3.09, q, 2H; 2.64, t, 2H; 2.18,

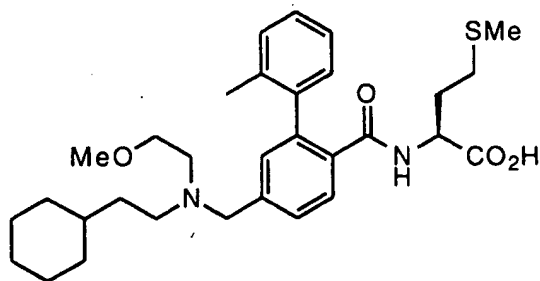


12070 s, 1.5 H (o-tolyl); 2.07, s, 1.5H (o-tolyl); 2.05, m, 1H; 2.03, s, 1.5H (MeS); 2.01, s, 1.5H (MeS); 1.87, m, 1H; 1.61, bm, 6H; 1.35, m, 2H; 1.20, m 2H; 1.14, m, 2H; 0.85, m, 2H.  
MS (ESI+): 579 (MH+); (ESI-): 577 (M-H).

Prepared according to the procedure of example 1178J.

12075 <sup>1</sup>H NMR (300 MHz., dmso d6): δ 7.52, d, 1H; 7.35, d, 1H; 7.23, m, 3H; 7.12, m, 3H; 6.91, d, 1H; 3.81, s, 2H; 3.66, m, 1H; 3.38, q, 2H; 2.56, t, 2H; 2.06, m, 1H; 2.00, bs, 3H; 1.92, s, 3H; 1.58, m, 7H; 1.00 - 1.38, m, 6H; 0.80, m, 2H.  
MS (ESI+): 587; 571; 565 (MH+); (ESI-): 563 (M-H). Calc'd for C<sub>30</sub>H<sub>38</sub>LiN<sub>2</sub>O<sub>3</sub>S•1.75 H<sub>2</sub>O; C 59.84; H 6.95; N 4.65; Found: C 59.86; H 6.57; N 4.45.

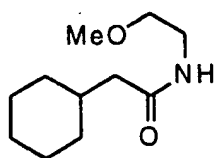
12080



Example 1104

N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

12085

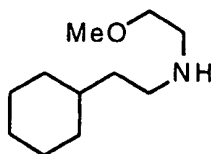


Example 1104A

N-(2-methoxyethyl)-2-cyclohexylacetamide

12090 The acid chloride from example 1178E (1.60 g, 10 mmol) in 10 mL of methylene chloride was added dropwise to a cold (0°C) solution of 2-methoxyethylamine (1.3 mL, 15 mmol) and pyridine (1.9 mL, 22 mmol) in 10 mL of methylene chloride and the mixture was stirred overnight. The mixture was diluted with ethyl ether and washed with water, 1M aqueous phosphoric acid, 2M aqueous sodium carbonate and brine, dried, filtered and concentrated to provide 1.70 g (85%) of the title compound as a white solid.

12095 <sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 5.89, bs, 1H; 3.46, m, 4H; 3.37, s, 3H; 2.05, d, 2H; 1.79, m, 1H; 1.70, bm, 6H; 1.24, m, 2H; 1.17, m, 1H; 0.95, m, 2H.  
MS (DCI, NH<sub>3</sub>): 200 (MH+).



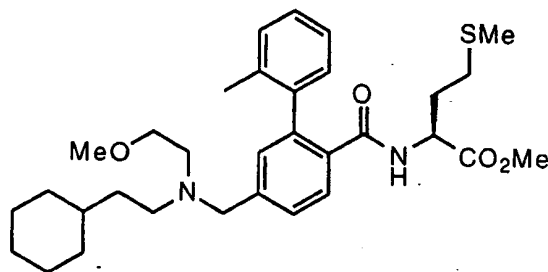
12100

Example 1104BN-(2-methoxyethyl)-N-2-cyclohexylethylamine

Using the procedure of example 1178F, example 1104A (1.70 g, 8.54 mmol) provided the title compound (1.56 g, 100%).

MS (DCI, NH<sub>3</sub>): 186 (MH<sup>+</sup>).

12105

Example 1104CN-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

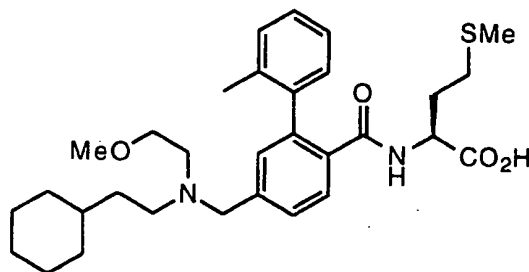
12110

Using the procedure of example 1103C, example 1104B (186 mg, 1.0 mmol) and example 403G (192 mg, 0.5 mmol) were combined to provide 78 mg (28%) of the title compound.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.91, dd, 1H; 7.42, dd, 1H; 7.18 - 7.37, m, 4H; 7.17, bs, 1H; 5.89, bd, 1H; 4.64, m, 1H; 3.68, s, 2H; 3.66, s, 3H; 3.45, t, 2H; 3.31, s, 3H; 2.66, t, 2H; 2.50, t, 2H; 2.19, s, 1.5H (o-tolyl); 2.07, s, 1.5H (o-tolyl); 2.05, m, 1H; 2.03, s, 1.5H (SMe); 2.01, s, 1.5H (SMe); 1.85, m, 1H; 1.63, bm, 6H; 1.34, m, 2H; 1.06 - 1.29, m, 4H; 0.88, m, 2H.

12115

MS (ESI<sup>+</sup>): 555 (MH<sup>+</sup>); (ESI<sup>-</sup>): 553 (M-H).



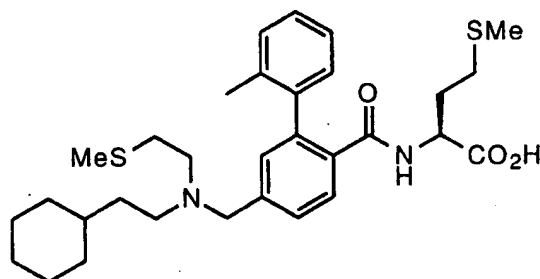
12120

Example 1104D

N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

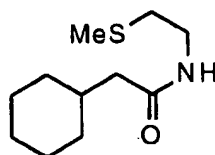
12125 A solution of example 1104C (73 mg, 0.13 mmol) in 2 mL of 3:1 THF/methanol was cooled in an ice bath and treated with lithium hydroxide (0.26 mL of a 1M aqueous solution, 0.26 mmol) and the mixture stirred overnight and then concentrated. The solid was diluted with water and the pH adjusted to 4.5 with 1M aqueous phosphoric acid and then extracted with 3 portions of ethyl acetate. The combined organic fractions were washed with brine, dried filtered and concentrated. The residue was lyophilized to provide 70 mg of the title  
12130 compound.

<sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.74, d, 1H; 7.58, d, 1H; 7.37, m, 1H; 7.10 - 7.31, m, 4H; 4.50, m, 3H; 3.66, t, 2H; 3.37, s, 3H; 3.22, t, 2H; 3.04, m, 2H; 2.22, bs, 1H; 2.10, m, 3H; 1.97, s, 3H; 1.90, m, 2H; 1.53 - 1.77, m, 8H; 1.14 - 1.38, m, 4H; 0.96, m, 2H.  
12135 MS (ESI+): 541 (MH+); (ESI-): 539 (M-H). Calc'd for C<sub>31</sub>H<sub>44</sub>N<sub>2</sub>O<sub>4</sub>S•0.85 H<sub>2</sub>O; C 66.96; H 8.28; N 5.04; Found: C 66.97; H 8.34; N 4.87.



Example 1105

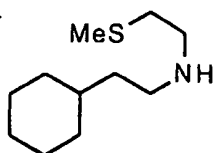
12140 N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



Example 1105A

12145 N-(2-methylthioethyl)-2-cyclohexylacetamide

Following the procedure of example 1104A, 2-methylthioethylamine (1.0 g, 11 mmol) was converted to the title compound (1.77 g, 89%).  
MS (DCI, NH<sub>3</sub>): 216 (MH<sup>+</sup>); 233 (M+NH<sub>4</sub>)<sup>+</sup>.

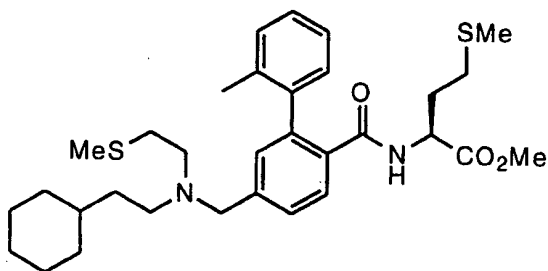


12150

Example 1105BN-(2-methylthioethyl)-2-cyclohexylethylamine

Using the procedure of example 1178F, example 1105A (1.75 g, 8.44 mmol) was converted into the title compound (1.63 g, 100%).

12155 MS (DCI, NH<sub>3</sub>): 202 (MH<sup>+</sup>).

Example 1105C

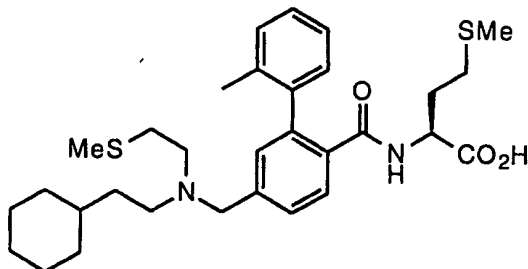
N-[4-(N-(2-cyclohexylethyl)-N-(2-methylthioethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

12160

Using the procedure of example 1103C, example 1105B (201 mg, 1.0 mmol) and example 403G (192 mg, 0.5 mmol) were combined to provide 151 mg (53%) of the title compound.

12165 <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.91, dd, 1H; 7.42, dd, 1H; 7.18 - 7.37, m, 4H; 7.17, bs, 1H; 5.89, bd, 1H; 4.63, m, 1H; 3.66, s, 3H; 3.63, s, 2H; 2.68, m, 2H; 2.59, m, 2H; 2.48, t, 2H; 1.99 - 2.21, m, 10H; 1.85, m, 1H; 1.62, bm, 6H; 1.36, m, 2H; 1.06 - 1.30, m, 4H; 0.87, m, 2H.

MS (ESI<sup>+</sup>): 571 (MH<sup>+</sup>); (ESI<sup>-</sup>): 569 (M-H).



12170

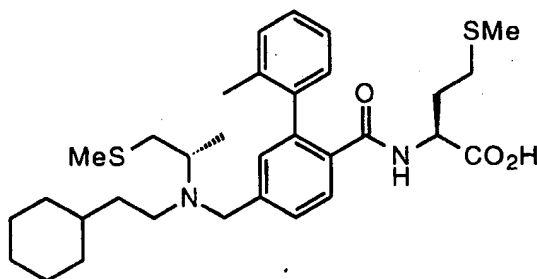
Example 1105D

N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

A solution of example 1105C (145 mg, 0.25 mmol) in 2 mL of 3:1 THF/methanol was cooled in an ice bath and treated with lithium hydroxide (0.5 mL of a 1M aqueous solution, 0.5 mmol) and the mixture stirred overnight. The solution was concentrated to dryness and diluted with water and the pH adjusted to 4.5 with 1M aqueous phosphoric acid. The solid collected was by filtration and dried in the air to provide 130 mg (93%) of the title compound.

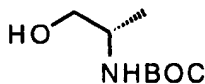
<sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.71, d, 1H; 7.57, d, 1H; 7.35, d, 1H; 7.10 - 7.31, m, 4H; 4.32, m, 1H; 4.17, s, 2H; 3.10, m, 2H; 2.94, m, 2H; 2.76, m, 2H; 2.22, bs, 1H; 2.02 - 2.09, m, 3H; 2.10, s, 3H; 1.99, s, 3H; 1.89, m, 2H; 1.68, m, 6H; 1.56, m, 2H; 1.09 - 1.26, m, 4H; 0.93, m, 2H.

MS (ESI+): 557 (MH<sup>+</sup>); (ESI-): 555 (M-H). Calc'd for C<sub>31</sub>H<sub>44</sub>N<sub>2</sub>O<sub>3</sub>S<sub>2</sub>•0.50 H<sub>2</sub>O; C 65.80; H 8.02; N 4.95; Found: C 65.79; H 7.89; N 4.79.



Example 1106

N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



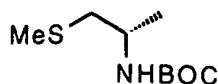
Example 1106A

2(S)-N-t-butoxycarbonylaminopropan-1-ol

A stirred solution of 2(S)-amino-1-propanol (1.0 g, 13.3 mmol) in 20 mL of methylene chloride was treated with di-tertbutyldicarbonate (3.19 g, 14.6 mmol) in 5 mL of methylene chloride and then the solution was treated with 10 mL of 2M aqueous sodium carbonate and stirred for 2 hours. The biphasic mixture was diluted with water and the layers were separated. The aqueous layer was extracted with methylene chloride and the combined organic layers were dried, filtered and concentrated to provide 2.35 g (105%) of the title compound.

<sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 4.59, bs, 1H; 3.77, m, 1H; 3.64, dd, 1H; 3.52, dd, 1H; 2.42, bs, 1H; 1.44, s, 9H; 1.14, d, 3H.

12205 MS (DCI, NH<sub>3</sub>): 176 (MH)<sup>+</sup>; 193 (M+NH<sub>4</sub>)<sup>+</sup>.



Example 1106B

1-Methylthio-2(S)-N-t-butoxycarbonylaminopropane

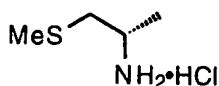
12210 A stirred solution of example 1106A (350 mg, 2.0 mmol) in 6 mL of methylene chloride was cooled in an ice/acetone bath and sequentially treated with triethylamine (0.34 mL, 2.4 mmol) and methanesulfonyl chloride (0.17 mL, 2.2 mmol) and the mixture stirred for 2 hours and then diluted with ether, extracted with water, 1M aqueous phosphoric acid, brine, dried filterd and concentrated to provide a yellow oil that was used directly. The

12215 mesylate was dissolved in 2 mL of DMF and added to a mixture of sodium thiomethoxide (280 mg, 4.0 mmol) and 5 mL of DMF and the mixture was stirred for 2 hours. The reaction was quenched by the addition of water and the mixture diluted with water and ethyl acetate. The layers were separated and the mixture was extracted with 2 additional portions of ethyl acetate and the combined organic layers washed with water and brine, dried, filtered and

12220 concentrated to provide 328 mg (80% overall) of the title compound.

<sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 3.86, bs, 1H; 2.65, dd, 1H; 2.56, dd, 1H; 2.14, s, 3H; 1.45, s, 9H; 1.22, d, 3H.

MS (DCI, NH<sub>3</sub>): 206 (MH)<sup>+</sup>; 223 (M+NH<sub>4</sub>)<sup>+</sup>.



12225

Example 1106C

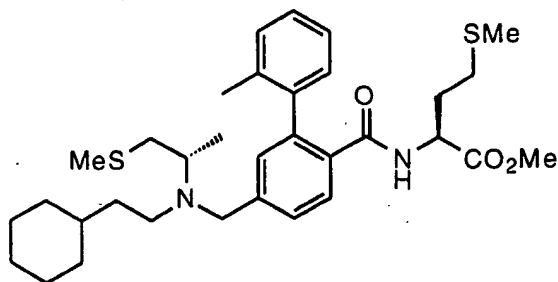
1-Methylthio-2(S)-aminopropane hydrochloride salt

Example 1106B (320 mg, 1.56 mmol) was dissolved in 2 mL of 4N HCl/dioxane and stirred for 1 Hour. The mixture was diluted with ether and filtered to provide 103 mg

12230 (53%) of the title compound as a white solid.

<sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 8.56, bs, 3H; 3.51, m, 1H; 2.89, dd, 1H; 2.78, dd, 1H; 2.17, s, 3H; 1.54, d, 3H.

MS (DCI, NH<sub>3</sub>): 123 (M+NH<sub>4</sub>)<sup>+</sup>.



12235

Example 1106DN-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

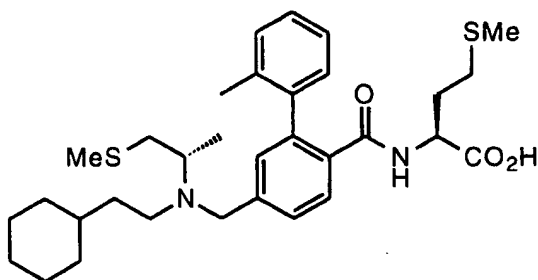
12240 Part 1. Following the general procedure of example 403H, example 1106C (98 mg, 0.69 mmol), example 403G (243 mg, 0.63 mmol), diisopropylethylamine (0.12 mL, 0.69 mmol) and acetic acid (0.18 mL, 3.14 mmol) were stirred in 4 mL of 1,2-dichloroethane for 2 hours and then treated with sodium triacetoxyborohydride (263 mg, 1.26 mmol). This procedure yielded 332 mg of material that was used in the next step.

12245 Part 2. The amine prepared in part 1 was treated with 2-cyclohexylacetaldehyde (159 mg, 1.26 mmol), acetic acid (0.36 mL, 6.3 mmol) and stirred for 2 hours. This solution was treated with sodium triacetoxyborohydride (263 mg, 1.26 mmol) and the mixture stirred overnight. The mixture was quenched and worked-up as described in example 403H. The residue obtained was purified by column chromatography on silica gel (20 g, 20% ethyl acetate/hexanes) to provide 225 mg (61% overall) of the title compound.

12250 <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.89, dd, 1H; 7.47, d, 1H; 7.15 - 7.37, m, 5H; 5.87, bd, 1H; 4.63, m, 1H; 3.67, d, 1H; 3.65, s, 3H; 3.55, d, 1H; 2.96, m, 1H; 2.75, dd, 1H; 2.44, m, 2H; 2.37, dd, 1H; 1.99 - 2.22, m, 10H; 1.84, m, 1H; 1.60, m, 6H; 1.09 - 1.33, m, 6H; 1.08, d, 3H; 0.72 - 1.00, m, 2H.

MS (ESI<sup>+</sup>): 585 (MH<sup>+</sup>); (ESI<sup>-</sup>): 583 (M-H).

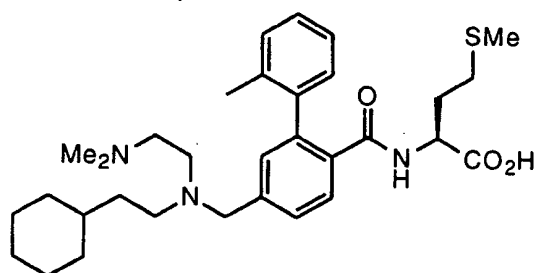
12255

Example 1106N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

12260 Following the procedure of example 1105D, example 1106D (210 mg, 0.36 mmol) provided 110 mg (53%) of the title compound.

<sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.69, d, 1H; 7.56, bd, 1H; 7.37, bd, 1H; 7.09 - 7.32, m, 4H; 4.33, m, 1H; 4.16, m, 1H; 4.00, m, 1H; 3.32, dt, 1H; 2.89, m, 3H; 2.64, m, 1H; 2.23, bs, 1H; 2.06, m, 2H; 2.04, s, 3H; 1.98, s, 3H; 1.89, m, 2H; 1.65, m, 6H; 1.44, m, 2H; 1.32, d, 3H; 1.28, m, 3H; 0.88, m, 2H.

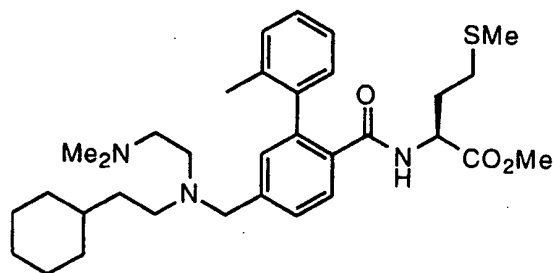
MS (ESI+): 571 (MH+); (ESI-): 569 (M-H). Calc'd for C<sub>32</sub>H<sub>46</sub>N<sub>2</sub>O<sub>3</sub>S<sub>2</sub>; C 67.33; H 8.12; N 4.91; Found: C 67.12; H 8.10; N 4.70.



12270

#### Example 1107

N-[4-(N-(2-cyclohexylethyl)-N-2,N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine



12275

#### Example 1107A

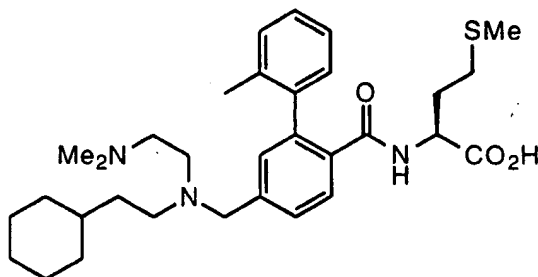
N-[4-(N-(2-cyclohexylethyl)-N-2,N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

12280 Part 1. Following the procedure of example 1106D, part 1, example 403G (550 mg, 1.43 mmol) and 2-N,N-dimethylaminoethylamine (0.31 mL, 2.86 mmol) and acetic acid (0.82 mL, 14.3 mmol) gave the corresponding secondary amine (673 mg).

Part 2. Following the procedure of example 1106D part 2, the amine produced in example 1107A, part 1 (660 mg, 1.44 mmol) and 2-cyclohexylacetaldehyde (364 mg, 2.88 mmol) gave a material that was purified by column chromatography on silica gel (25 g, ethyl



- 12285 acetate then 90/10/0.1 ethyl acetate/methanol/conc. aq. ammonia) providing 498 mg (60% overall) of the title compound.  
<sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 7.90, dd, 1H; 7.41, dd, 1H; 7.18 - 7.34, m, 4H; 7.16, bs, 1H; 5.88, bs, 1H; 4.62, m, 1H; 3.65, s, 3H; 3.63, s, 2H; 2.57, m, 2H; 2.47, m, 2H; 2.39, m, 2H; 2.21, s, 6H; 1.99, 2.28, m, 7H; 1.86, m, 1H; 1.63, bm, 6H; 1.35, m, 2H; 1.20 m, 2H; 1.14, m, 2H; 0.85, m, 2H.  
 12290 MS (ESI+): 568 (MH+); (ESI-): 566 (M-H).  
 MS (ESI+): 568 (MH+); (ESI-): 566 (M-H).



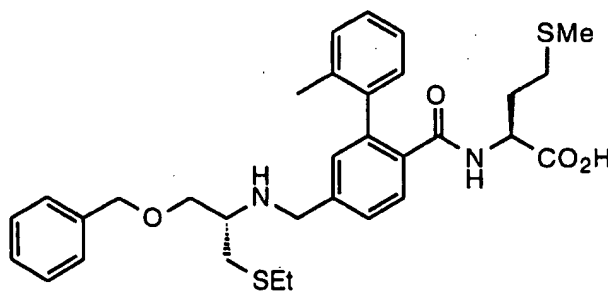
#### Example 1107B

- 12295 N-[4-(N-(2-cyclohexylethyl)-N-2,N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1104D, example 1107A (485 mg, 0.85 mmol) provided 382 mg (81%) of the title compound as a white lyophilate.

- <sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.66, d, 1H; 7.46, d, 1H; 7.05 - 7.33, m, 5H; 4.35, m, 1H; 3.74, s, 2H; 3.17, t, 1H; 2.82, t, 2H; 2.75, s, 6H; 2.60, m, 2H; 2.24, bs, 1H; 1.94 - 2.12, m, 6H; 1.85, m, 2H; 1.67, m, 6H; 1.45, m, 2H; 1.21, m, 4H; 0.92, m, 2H.  
 12300 MS (ESI+): 554 (MH+); (ESI-): 552 (M-H). Calc'd for C<sub>32</sub>H<sub>47</sub>N<sub>3</sub>O<sub>3</sub>S•1.00 H<sub>2</sub>O; C 67.22; H 8.64; N 7.35; Found: C 67.23; H 8.43; N 7.26.

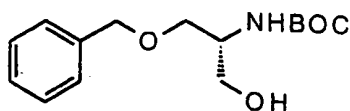
12305



#### Example 1108

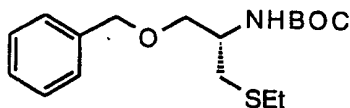
- N-[4-(N-(1-benzyloxymethyl-2(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

12310

Example 1108A1-benzyloxy-2(S)-t-butoxycarbonylamino-3-hydroxypropane

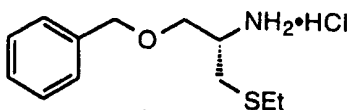
N-BOC-O-benzylserine (5.0 g, 16.9 mmol) in 30 mL dimethoxyethane was treated with 4-methylmorpholine (2.0 mL, 18.6 mmol) and cooled to 0°C. The solution was treated with isobutylchloroformate (2.3 mL, 17.8 mmol) and the resulting suspension stirred for 15 minutes, then filtered. The solids collected were washed with 2 portions of dimethoxyethane and the washings combined with the original filtrate. This material was cooled in an ice bath and treated with a cold solution of sodium borohydride (1.93 g, 50.8 mmol) in 40 mL 1/2 saturated sodium bicarbonate and the reaction stirred for 2 hours. The mixture was diluted with water and extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with saturated aqueous sodium bicarbonate, water and brine, dried, filtered and concentrated to provide the title compound.

MS (DCI, NH<sub>3</sub>): 282 (MH<sup>+</sup>); 299 (M+NH<sub>4</sub>)<sup>+</sup>.

Example 1108B1-benzyloxy-2(S)-t-butoxycarbonylamino-3-ethylthiopropene

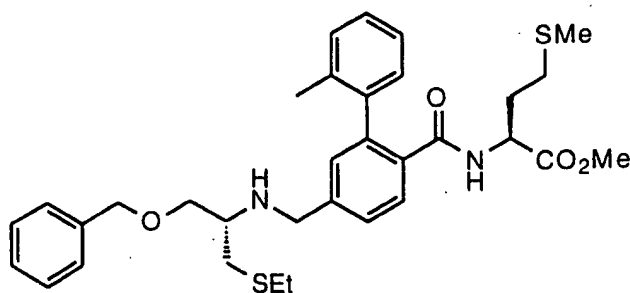
Following the procedure described in example 1106B (and substituting potassium thioethoxide for sodium thiomethoxide), example 1108A (322 mg, 1.5 mmol) was converted to 342 mg (70% overall) the title compound.

MS (DCI, NH<sub>3</sub>): 326 (MH<sup>+</sup>); 343 (M+NH<sub>4</sub>)<sup>+</sup>.

Example 1108B1-benzyloxy-2(S)-amino-3-ethylthiopropene hydrochloride salt

Following the procedure described in example 1106C, example 1108B (342 mg, 1.05 mmol) was converted to 244 mg (89%) of the title compound.

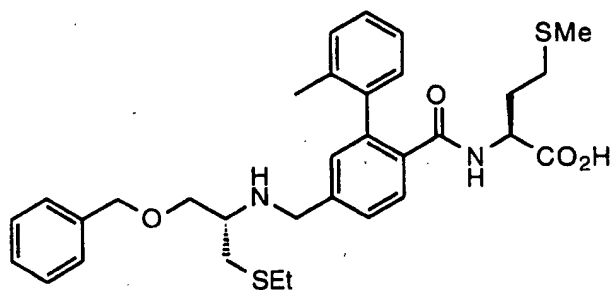
MS (DCI, NH<sub>3</sub>): 226 (MH<sup>+</sup>).

Example 1108C

N-[4-(N-(1-benzyloxymethyl-2(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

12345 Following the procedure described in example 1106D, part 1, example 1108C (144 mg, 0.55 mmol), example 403G (192 mg, 0.50 mmol), diisopropylethylamine (0.098 mL, 0.55 mmol) and acetic acid (0.14 mL, 2.5 mmol) and sodium triacetoxyborohydride (213 mg, 1.0 mmol) provided 196 mg (66%) of the title compound after chromatography (silica gel, 20 g, 50% ethyl acetate/hexanes).

12350 MS (ESI+): 595 (MH+); (ESI-): 593 (M-H).

Example 1108D

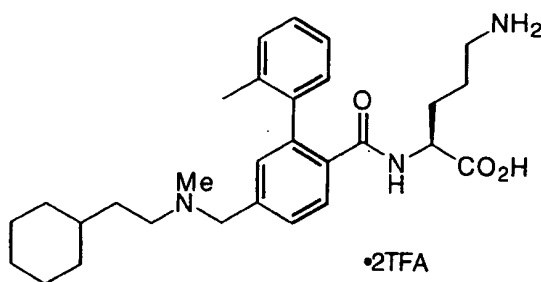
N-[4-(N-(1-benzyloxymethyl-2(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

12355 Following the procedure of example 1104D, example 1108C (187 mg, 0.31 mmol) provided 175 mg of the title compound.

<sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD): δ 7.70, d, 1H; 7.50, d, 1H; 7.08 - 7.39, m, 10H; 4.59, s, 2H; 4.29, m, 1H; 4.20, s, 2H; 3.70, d, 2H; 3.37, m, 1H; 2.85, d, 2H; 2.49, m, 2H; 2.21, bs, 1.5H; 2.08, s, 1.5H; 2.03, m, 1H; 1.98, s, 3H; 1.87, m, 2H; 1.68, m, 1H; 1.20, t, 3H.

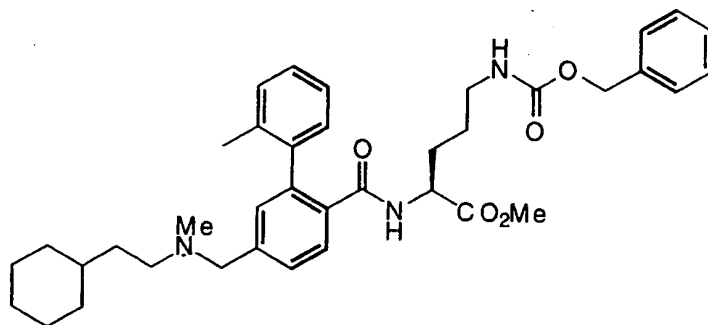
12360 MS (ESI+): 581 (MH+); (ESI-): 579 (M-H). Calc'd for C<sub>32</sub>H<sub>40</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>; C 66.18; H 6.94; N 4.82; Found: C 65.52; H 6.76; N 4.58.

12365

Example 1110

N-[4-(N-(2-Cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]ornithine,  
Trifluoroacetate salt

12370

Example 1110A

N-[4-(N-(2-Cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]-N'-  
carbobenzyloxyornithine, Methyl Ester

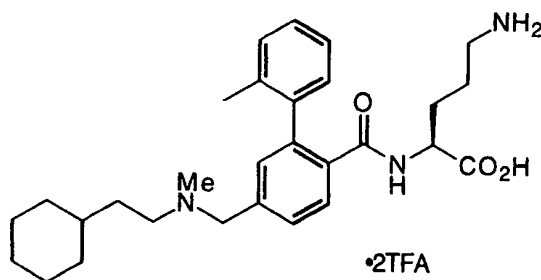
12375

The title compound was prepared according to the procedure in example 608D, replacing L-methionine methyl ester-HCl with L-N'-carbobenzyloxyornithine methyl ester-HCl, and was isolated as a colorless oil.

MS (ESI(+)) m/e 628 (M+H)<sup>+</sup>.

MS (ESI(-)) m/e 626 (M-H)<sup>-</sup>.

12380

Example 1110B

N-[4-(N-(2-Cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]ornithine,  
Trifluoroacetate salt

12385 To a solution of N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]-N'-carbobenzyloxyornithine methyl ester (270mg) in methanol (1.4mL) was added 5M LiOH (0.103mL). After 4h, the reaction was concentrated and the residue was dissolved in ethanol (3mL), followed by the addition of freshly distilled cyclohexene (0.1mL), then 10% palladium on carbon (50mg). The reaction vessel was

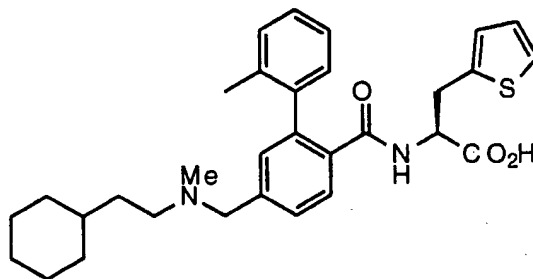
12390 tightly sealed and warmed to 80°C for 1h. Analytical HPCL analysis indicates ca. 30% conversion to the title compound. The reaction was filtered and concentrated, and the hydrogenation protocol was repeated twice. Analytical HPCL analysis of the resulting mixture still indicated low conversion. The reaction was filtered and concentrated, and the residue was dissolved in a minimum of 10%methanol/water, and purified by preparative

12395 reverse-phase medium pressure liquid chromatography, eluting with a gradient of methanol/water/0.1%TFA. Lyophilization of the appropriate fractions afforded the title compound as a light yellow powder (38mg).

<sup>1</sup>H NMR (300 MHz, DMSO) δ 0.83-0.97 (m, 2H), 1.08-1.83 (m, 15H), 2.07-2.14 (m, 4H), 2.62-2.73 (m, 4H), 2.95-3.24 (m, 2H), 4.09-4.17 (m, 1H), 4.22-4.49 (m, 2H),

12400 7.09-7.27 (m, 4H), 7.40 (s, 1H), 7.54-7.73 (m, 5H), 8.40 (brd, J=5 Hz, 1H), 9.68 (brs, 1H).

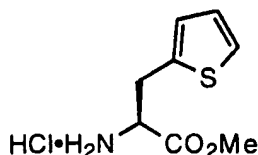
MS (APCI(-)) m/e 478 (M-H).



12405

Example 1112

N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine



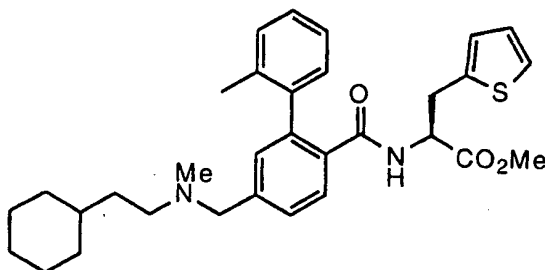
12410

Example 1112A

3-(2-thienyl)-L-alanine, methylester hydrochloride

12415 A solution of 3-(2-thienyl)-L-alanine (200 mg, 1.17 mmol) in 3 mL of methanol was treated with chlorotrimethylsilane (0.73 mL, 5.84 mmol) and the mixture heated to reflux for 60 hours. The solution was then concentrated to provide 257 mg (99%) of the title compound.

MS (DCI, NH<sub>3</sub>): 186 (MH<sup>+</sup>); 203 (M+NH<sub>4</sub>)<sup>+</sup>.



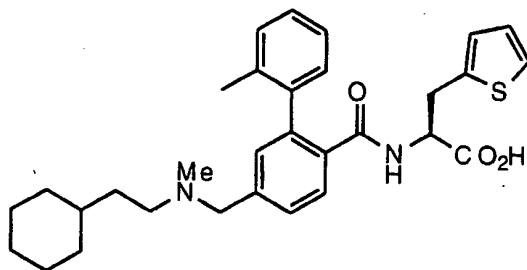
12420

#### Example 1112B

#### N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine

12425 Following the procedure of example 608D, example 1112A (122 mg, 0.55 mmol) and example 608C (183 mg, 0.5 mmol) were converted to 154 mg (58%) of the title compound.

MS (ESI<sup>+</sup>): 533 (MH<sup>+</sup>); (ESI<sup>-</sup>): 531 (M-H).



#### Example 1112C

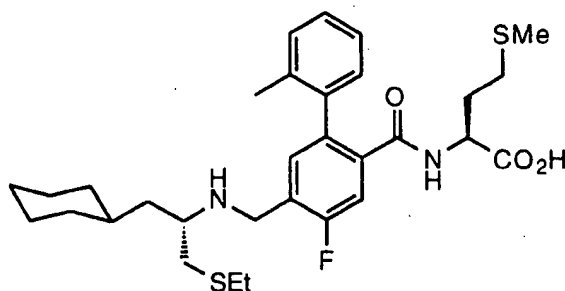
#### N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine

12430 Following the procedure of example 1105D, example 1112C (150 mg, 0.28 mmol) provided 124 mg (85%) of the title compound.

12435 <sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.69, m, 1H; 7.52, dd, 1H; 7.31, bs, 1H; 7.21, m, 2H; 7.14, m, 3H; 6.85, bt, 1H; 6.72, m, 1H; 4.40, m, 1H; 4.24, bd, 2H; 3.10 - 3.27, m, 2H; 3.06, m, 2H; 2.72, s, 3H; 2.08, s, 3H; 1.56 - 1.76, m, 7H; 1.13 - 1.37, m, 4H; 0.96, m, 2H.

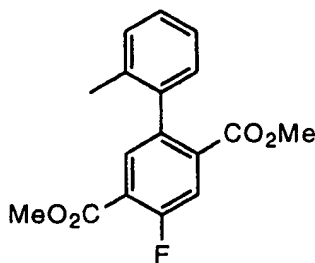
MS (ESI+): 519 (MH<sup>+</sup>); (ESI-): 517 (M-H). Calc'd for C<sub>31</sub>H<sub>38</sub>N<sub>2</sub>O<sub>3</sub>S•0.75 H<sub>2</sub>O; C 69.96; H 7.48; N 5.26; Found: C 70.01; H 7.38; N 5.19.

12440

Example 1134

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine

12445

Example 1134A

Dimethyl 2-(2-Methylphenyl)-5-fluoroterephthalate

12450

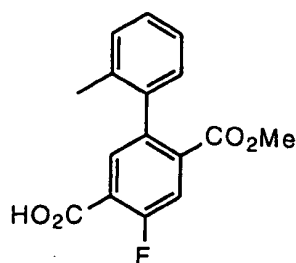
A stirred solution of the product from example 319B (2.99 g, 10.00 mmol) in 30 ml of dioxane was cooled in an ice bath and 6.5 ml of a 48% aqueous solution of tetrafluoroboric acid was added. The resulting solution was treated with t-butylnitrite such that the internal temperature did not exceed 10°C and stirring was continued for 30 minutes further. The mixture was carefully diluted with ether (~200 mL) and the solid collected by filtration. The dried solid was suspended in 20 mL of isooctane and heated to reflux overnight and then diluted with 5 mL of dioxane and heating continued for 1 hour more. The resulting dark mixture was cooled to ambient temperature and concentrated. The residue was purified by column chromatography on silica gel (50g, 5% ethyl acetate/hexanes) to provide 0.87 g (29%) of the title compound.

12455

12460

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.73, d, 1H; 7.72, d, 1H; 7.15 - 7.32, m, 3H; 7.06, d, 1H; 3.94, s, 3H; 3.65, s, 3H; 2.07, s, 3H.

MS (DCI-NH<sub>3</sub>): 320 (M+NH<sub>4</sub>H<sup>+</sup>).



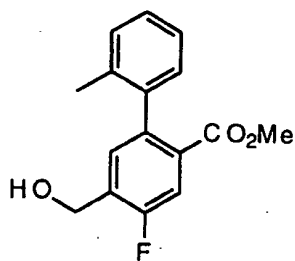
Example 1134B

2-(2-Methylphenyl)-4-carboxy-5-fluorobenzoic acid, methyl ester

A solution of example 1134A (0.87 g, 2.88 mmol) in 10 mL of 4:1 THF/methanol was treated with 3 mL of 1M aqueous lithium hydroxide and the mixture stirred at ambient temperature for 60 hours. The solution was made acidic by the addition of excess 3N aqueous HCl and then extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with water and brine, dried, filtered and concentrated to provide 0.77 g (92%) of the title compound sufficiently pure to use in the next step.

<sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.74, d, 1H; 7.69, d, 1H; 7.15 - 7.28, m, 3H; 7.03, q, 1H; 3.61, s, 3H; 2.07, s, 3H.

MS (DCI, NH<sub>3</sub>): 306 (M+ NH<sub>4</sub><sup>+</sup>).



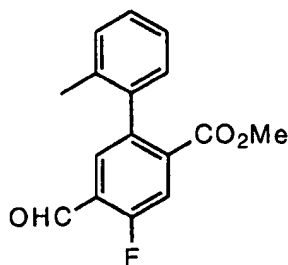
Example 1134C

2-(2-Methylphenyl)-4-hydroxymethyl-5-fluorobenzoic acid, methyl ester

A solution of example 1134B (760 mg, 2.64 mmol) in 5 mL of dimethoxyethane was treated with 4-methylmorpholine (0.32 mL, 2.90 mmol) and the mixture cooled in an ice bath. The clear solution was then treated with isobutylchloroformate (0.36 mL, 2.77 mmol) and the suspension stirred for 30 minutes. The mixture was filtered and the solids washed with 2 portions of THF and the combined filtrates recooled in an ice bath. The cold solution was treated with a mixture of sodium borohydride (300 mg, 7.92 mmol) in 3 mL of 1/2 saturated sodium bicarbonate and the mixture stirred for 2 hours. The mixture was diluted with water and extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with water and brine, dried, filtered and concentrated. The residue was purified by column chromatography of silica gel (35 g, 25% ethyl acetate/hexanes) to provide 527 mg (73%) of the title compound.



$^1\text{H}$  NMR (300 MHz.,  $\text{CDCl}_3$ ):  $\delta$  7.67, d, 1H; 7.44, d, 1H; 7.15 - 7.28, m, 3H; 7.05, d, 1H; 4.83, d, 1H; 3.62, s, 3H; 2.07, s, 3H; 1.94, bt, 1H.  
MS (DCI,  $\text{NH}_3$ ): 292 ( $\text{M} + \text{NH}_4^+$ ).



12495

Example 1134D2-(2-Methylphenyl)-4-formyl-5-fluorobenzoic acid, methyl ester

A stirred solution of example 1134C (515 mg, 1.79 mmol) in 2 mL of methylene chloride was treated with KBr (21 mg, 0.18 mmol), 2 mL of water and sodium bicarbonate (0.5 g) and then cooled in an ice bath. The mixture was treated with TEMPO (3 mg, 0.02 mmol) and then commercial bleach (Chlorox, 3.1 mL) was added such that the temperature did not exceed  $5^\circ\text{C}$ . The mixture was stirred for 10 minutes at which time an additional 1.5 mL of Chlorox was added. After stirring a further 10 minutes, the mixture was diluted with water and layers were separated. The aqueous phase was extracted with 1 portion of methylene chloride and the combined organic phases were extracted with 5% aqueous sodium bisulfite, dried, filtered and concentrated to give 478 mg (93%) of the title compound.

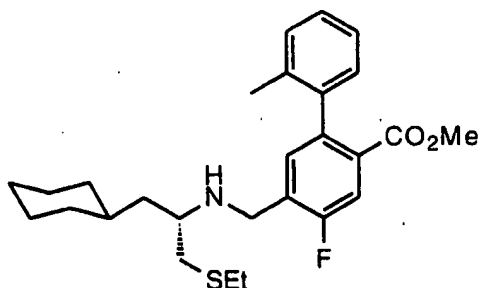
12500

12505

$^1\text{H}$  NMR (300 MHz.,  $\text{CDCl}_3$ ):  $\delta$  10.43, s, 1H; 7.77, d, 1H; 7.73, d, 1H; 7.17 - 7.31, m, 3H; 7.05, m, 1H; 3.63, s, 3H; 2.06, s, 3H.

12510

MS (DCI,  $\text{NH}_3$ ): 290 ( $\text{M} + \text{NH}_4^+$ ).

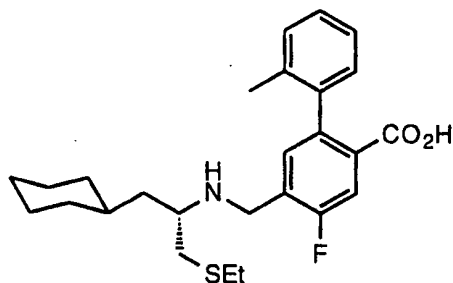
Example 1134EN-[4-(1-ethylthio-3-cyclohexyl)prop-2-ylaminomethyl]-5-fluoro-2-(2-methylphenyl)benzoic acid methyl ester

12515

Example 1134D (143 mg, 0.5 mmol) was dissolved in 2 mL of 1,2-dichloroethane and the amine hydrochloride salt from example 403D (178 mg, 0.75 mmol), diisopropylethylamine (0.13 mL, 0.75 mmol) and acetic acid (0.15 mL, 2.50 mmol) were sequentially added. The mixture was stirred at ambient temperature for 4 hours and then treated with sodium triacetoxyborohydride (213 mg, 1.0 mmol) and the mixture stirred overnight. The reaction was quenched by the addition of 2 mL of 2M aqueous sodium carbonate and the mixture stirred vigorously for 1 hour and then diluted with water and methylene chloride. The aqueous layer was extracted with methylene chloride and the combined organic layers dried, filtered and concentrated. The residue was purified by column chromatography on silica gel (20g, 15% ethyl acetate/hexanes) to provide 165 mg (72%) of the title compound.

<sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 7.67, d, 1H; 7.16 - 7.31, m, 5H; 7.04, bd, 1H; 3.93, s, 2H; 3.63, s, 3H; 2.76, m, 2H; 2.57, m, 1H; 2.46, q, 2H; 2.06, s, 3H; 1.63, bm, 6H; 1.37, bm, 3H; 1.22, t, 3H; 1.13, m, 2H; 0.87, m, 2H.

MS (ESI +): 458 (MH<sup>+</sup>); (ESI-) 456 (M-H).

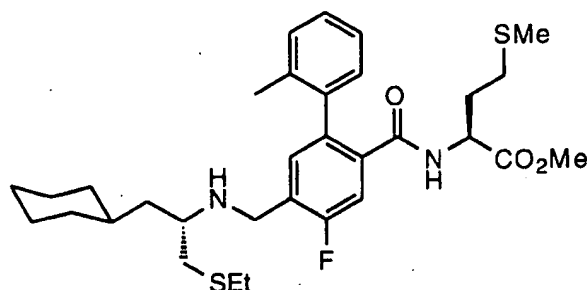


Example 1134F

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoic acid

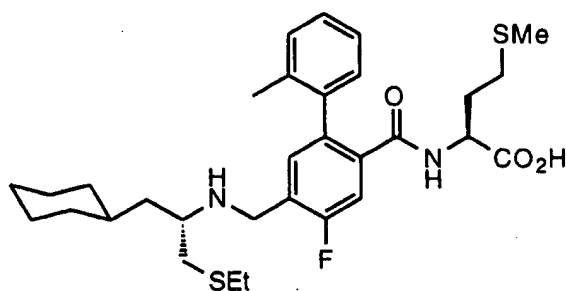
Example 1134E (160 mg, 0.35 mmol) was dissolved in 1.5 mL of ethanol and aqueous sodium hydroxide was added (1.75 mL of a 4N solution) and the mixture heated to reflux for 3 hours. The cooled solution was concentrated to dryness and dissolved in water and the pH adjusted to ~ 4 with 1M aqueous phosphoric acid. The mixture was extracted with 3 portions of ethyl acetate and the combined organic extracts were washed with brine, dried, filtered and concentrated to provide 164 mg (105%) of the title compound.

<sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.78, d, 1H; 7.43, d, 1H; 7.15 - 7.27, m, 3H; 7.06, bd, 1H; 4.42, m, 2H; 3.48, m, 1H; 3.00, dd, 1H; 2.93, dd, 1H; 2.58, q, 2H; 2.09, s, 3H; 1.63 - 1.79, m, 7H; 1.45, bm, 2H; 1.14 - 1.36, m, 6H; 0.84 - 1.09, m, 2H.

Example 1134G

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine, methyl ester

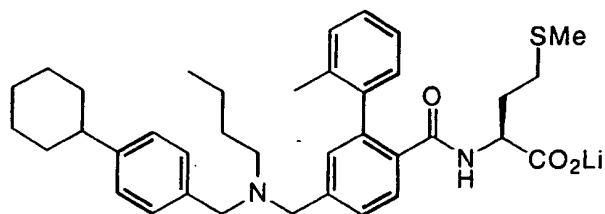
12550 According to the procedure described in example 1178I, example 1134F (160 mg, 0.35 mmol) provided 140 mg (68%) of the title compound after column chromatographic purification on silica gel (20 g, 35% ethyl acetate/hexanes).  
<sup>1</sup>H NMR (300 MHz., CDCl<sub>3</sub>): δ 7.70, dd, 1H; 7.14 - 7.38, m, 5H; 5.91, bd, 1H; 4.60, m, 1H; 3.94, s, 2H; 3.66, s, 3H; 2.77, m, 2H; 2.58, m, 1H; 2.46, q, 2H; 2.28, s, 1.5 H(o-tolyl rotamer); 2.07, s, 1.5H (o-tolyl rotamer); 1.95 - 2.10, m, 5H; 1.84, m, 2H; 1.50 - 1.72, m, 6H; 1.26 - 1.48, m, 3H; 1.21, t, 3H; 1.04 - 1.26, m, 3H; 0.88, m, 2H. MS: (ESI-): 587 (M-H).

Example 1134H

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine

Following the procedure of example 1105D, example 1134G (130 mg, 0.22 mmol) provided 94 mg (75%) of the title compound.

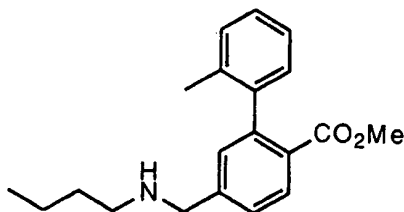
12565 <sup>1</sup>H NMR (300 MHz., CD<sub>3</sub>OD): δ 7.52, d, 1H; 7.39, m, 1H; 7.10 - 7.30, m, 4H; 4.29, m, 1H; 4.25, q, 2H; 3.24, m, 1H; 2.89, dd, 1H; 2.78, dd, 1H; 2.52, q, 2H; 2.22, bs, 1.5H; 2.08, bs, 1.5H; 2.05, m, 1H; 1.98, s, 3H; 1.89, m, 2H; 1.69, m, 6H; 1.58, t, 2H; 1.43, m, 1H; 1.25, m, 1H; 1.22, t, 3H; 0.90, m, 2H.  
 MS (ESI+): 575 (MH+); (ESI-): 573 (M-H). Calc'd for C<sub>31</sub>H<sub>43</sub>FN<sub>2</sub>O<sub>3</sub>S<sub>2</sub>•0.35 H<sub>2</sub>O; C 64.07; H 7.58; N 4.82; Found: C 64.08; H 7.54; N 4.65.



12575

Example 1136

N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine  
lithium salt

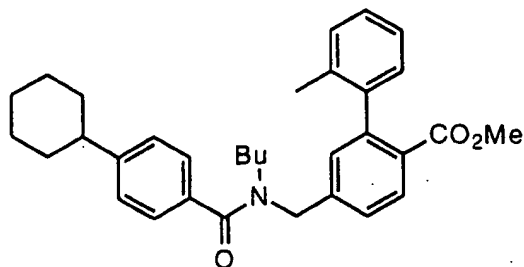


12580

Example 1136A

Methyl 4-(N-Butylaminomethyl)-2-(2-methylphenyl)benzoate

To a 0 °C solution of intermediate 1178B (1.0 g, 3.71 mmol) in DCM (10 mL) was added oxalyl chloride (2.0 M in DCM, 3.7 mL), and a drop of DMF. The reaction was stirred at room temperature for 2 hours, and was then evaporated to dryness. The residue was redissolved in DCM (10 mL), and was cooled to 0 °C. To it was slowly added butylamine (0.5 mL). The reaction mixture was stirred for 5 min., and then was filtered through silica gel (10 g), rinsed with ethyl acetate, and concentrated. The solid was dissolved in THF (10 mL), and to it was added borane (1.0 M in THF, 5.0 mL), and the reaction mixture was refluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (1 mL), and the mixture was heated at 60 °C for 1 hour. Then it was cooled to room temperature, the reaction mixture was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the intermediate amine. The amine was used without further purification.

**Example 1136B****Methyl 4-[N-butyl-N-(4-cyclohexylbenzylcarbonyl)aminomethyl]-2-(2-methylphenyl)benzoate**

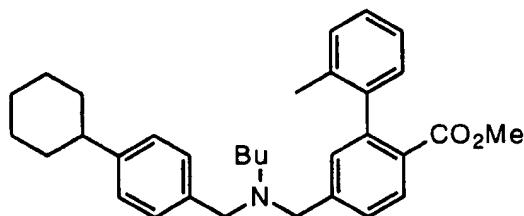
12600

12605

12610

To a 0 °C solution of 4-cyclohexylbenzoic acid (204 mg, 1.0 mmol) in DCM (3 mL) was added oxalyl chloride (2.0 M in DCM, 1.0 mL), and a drop of DMF. The reaction was stirred at room temperature for 2 hours, and was then evaporated to dryness. The residue was redissolved in DCM (10 mL), and was cooled to 0 °C. To it was slowly added the intermediate 1136A (156 mg, 0.5 mmol) and triethylamine (202 mg, 2.0 mmol) in DCM (3 mL). The reaction mixture was stirred for 5 min., and then was filtered through silica gel (10 g), rinsed with ether, and concentrated. The residue was purified by column chromatography with 20% ethyl acetate in to give the title compound (165 mg, 66%).

<sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.95 (d, 1 H), 7.32-7.16 (m, 9 H), 7.05 (br d, 1 H), 5.85-5.55 (loop, 2 H), 3.61 (s, 3 H), 3.47-3.17 (broad loop, 2 H), 2.49 (m, 1 H), 2.06 (s, 3 H), 1.90-0.70 (m, 17 H). MS(CI/NH<sub>3</sub>) m/z: 498 (M+H)<sup>+</sup>.

**Example 1136C**

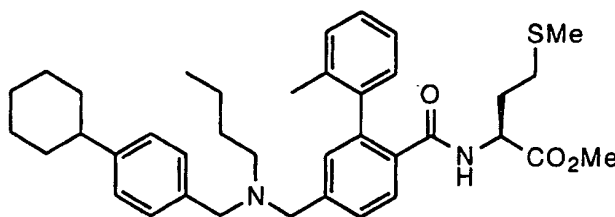
12615

12620

**Methyl 4-(N-Butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoate**

To a solution of intermediate 1136B (93 mg) in THF (2 mL) was added borane (1.0 M in THF, 1.0 mL), and the reaction mixture was refluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. Then it was cooled to room temperature, and was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the title amine (88 mg, 94%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)

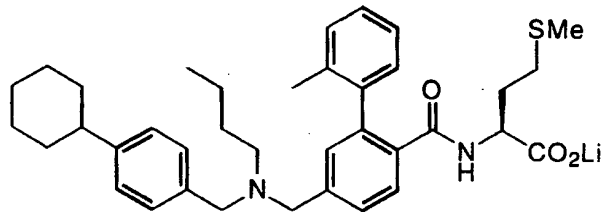
12625  $\delta$  7.90 (d, 1 H), 7.42 (dd, 1 H), 7.30-7.15 (m, 4 H), 7.12 (m, 2 H), 7.06 (m, 1 H), 3.59 (s, 2 H), 3.57 (br s, 2 H), 3.53 (br s, 2 H), 2.47 (m, 1 H), 2.41 (t, 2 H), 2.05 (s, 3 H), 1.90-1.20 (m, 14 H), 0.94 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 484 (M+H)<sup>+</sup>.



#### Example 1136D

12630 N-[4-(N-Butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

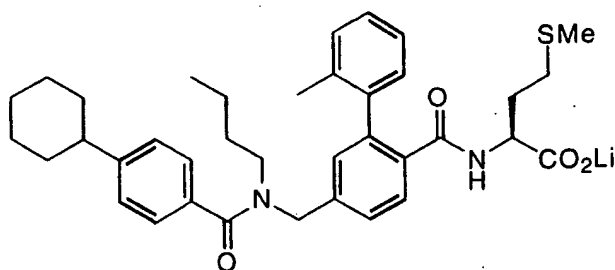
The procedures described in the Example 403E and 403F were used here to convert above intermediate 1136C (85 mg) to the title methyl ester 1136D (73 mg, 68%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.90 (2 d's 1 H), 7.45 (br d, 1 H), 7.35-7.22 (m, 6 H), 7.19 (br s, 1 H), 7.13 (br d, 2 H), 5.85 (m, 1 H), 4.62 (m, 1 H), 3.65 (s, 3 H), 3.57 (s, 2 H), 3.53 (s, 2 H), 2.48 (m, 1 H), 2.41 (t, 2 H), 2.20-2.00 (4 s's, 6 H), 2.05 (m, 2 H), 1.92-1.20 (m, 16 H), 0.82 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 615 (M+H)<sup>+</sup>.



#### Example 1136E

12640 N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

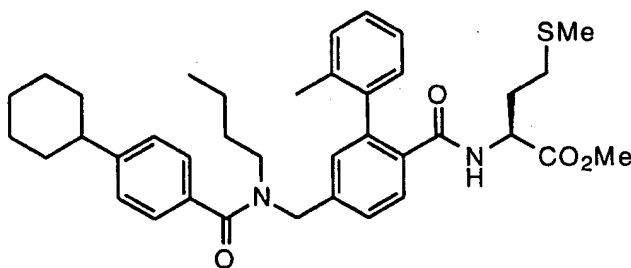
The procedure described in the Example 403I was used here to convert the intermediate 1136D (64 mg) to the title lithium salt (64 mg, 100%). <sup>1</sup>H NMR (300 MHz, dms<sub>o</sub>-d<sub>6</sub>)  $\delta$  7.49 (d, 1 H), 7.37 (br d, 1 H), 7.25-7.09 (m, 9 H), 6.91 (d, 1 H), 3.63 (m, 1 H), 3.56 (br s, 2 H), 3.47 (br s, 2 H), 2.45 (m, 1 H), 2.37 (t, 2 H), 2.17-1.98 (m, 8 H), 1.81-1.17 (m, 16 H), 0.76 (t, 3 H). MS(ESI-) m/z: 599 (M-H)<sup>-</sup>.



12650

Example 1137

N-[4-(N-Butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine  
lithium salt



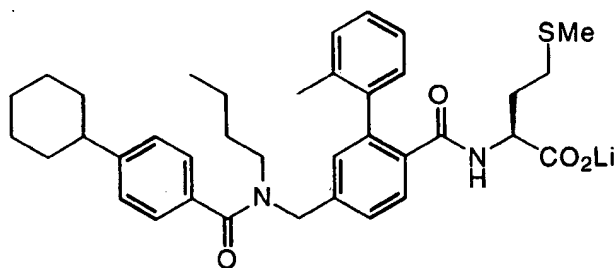
12655

Example 1137A

N-[4-(N-butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine  
Methyl Ester

The procedures described in the Example 403E and 403F were used here to convert intermediate 1136B (63 mg) to the title methyl ester 1137A (72 mg, 90%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.94 (2 d's 1 H), 7.37-7.15 (m, 10 H), 5.89 (m, 1 H), 4.80 (m, 1 H), 4.61 (br. loop, 2 H), 3.66 (s, 3 H), 3.43, 3.22 (2 br loops, 2 H), 2.50 (m, 1 H), 2.20-2.00 (m, 8 H), 1.92-1.00 (m, 16 H), 0.96-0.70 (2 br loops, 3 H). MS(CI/NH<sub>3</sub>) m/z: 629 (M+H)<sup>+</sup>.

12660



12665

Example 1137B

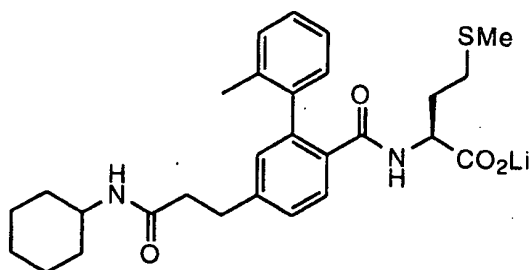
N-[4-(N-Butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine  
lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1137B (68 mg) to the title lithium salt (67 mg, 100%). <sup>1</sup>H NMR (300 MHz,

12670

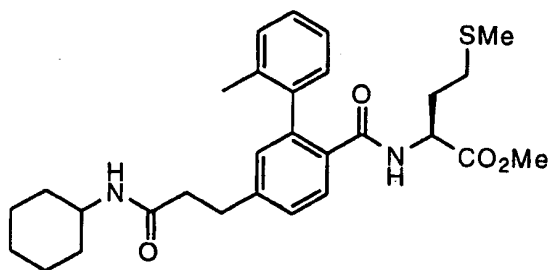
dmso-d<sub>6</sub>)  $\delta$  7.53 (br d, 1 H), 7.42-7.08 (m, 9 H), 6.97 (m, 1 H), 6.95 (br d, 1 H), 4.72, 4.57 (2 br. loops, 2 H), 3.65 (m, 1 H), 3.17 (br loop, 2 H), 2.50 (m, 1 H), 2.20-1.88 (m, 8 H), 1.86-0.95 (m, 16 H), 0.88, 0.67 (2 br loops, 3 H). MS(ESI-) m/z: 613 (M-H)<sup>-</sup>

12675

Example 1139

N-[4-(N-Cyclohexylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl-L-methionine lithium salt

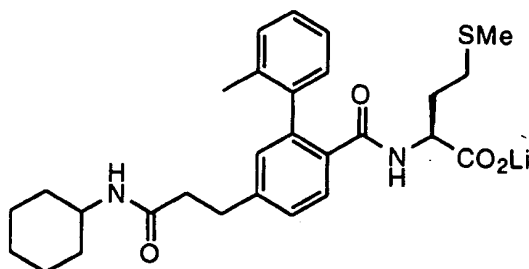
12680

Example 1139 A

N-[4-(N-Cyclohexylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl-L-methionine lithium salt

12685

The procedures described in the Example 403E and 403F were used here to convert intermediate 1144C (127 mg) to the title methyl ester (141 mg, 83%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.89 (2 d's, 1 H), 7.32-7.24 (m, 4 H), 7.95 (br d, 1 H), 7.03 (br s, 1 H), 5.86 (br d, 1 H), 5.16 (m, 1 H), 4.62 (m, 1 H), 3.75 (m, 1 H), 3.02 (t, 2 H), 2.45 (t, 2 H), 2.20-2.00 (m, 8 H), 1.92-0.97 (m, 12 H).

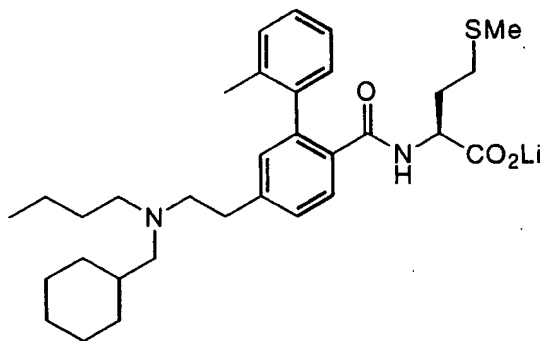
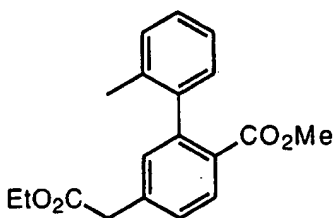


12690



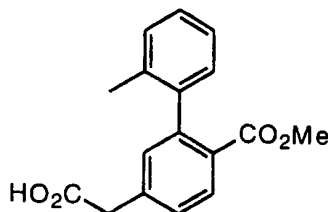
Example 1139BN-[4-(N-Cyclohexylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1139A (134 mg) to the title lithium salt (121 mg, 93%). <sup>1</sup>H NMR (300 MHz, dmsd-d<sub>6</sub>) δ 7.67 (d, 1 H), 7.45 (d, 1 H), 7.27-7.08 (m, 5 H), 6.97 (m, 1 H), 6.88 (m, 1 H), 3.66 (m, 1 H), 2.85 (t, 2 H), 2.36 (t, 2 H), 2.00-1.90 (m, 8 H), 1.88-0.98 (m, 12 H). MS(ESI-) m/z: 495 (M-H)<sup>-</sup>.

Example 1140N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium saltExample 1140AMethyl 4-(Ethoxycarbonylmethyl)-2-(2-methylphenyl)benzoate

A solution of intermediate 1178D (397 g, 1.24 mmol), palladium(II) acetate (22 mg), 1,3-bis(diphenylphosphino)propane (42 mg), N,N-diisopropylethylamine (0.5 mL) in ethanol (1 mL) and DMF (5 mL) was stirred at 80 °C under carbon monoxide balloon for 4 hours. The reaction mixture was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 5% ethyl acetate in hexane to give the title compound (233 mg, 58%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.94 (d, 1 H), 7.35 (dd, 1 H), 7.30-7.17 (m, 3

H), 7.16 (d, 1 H), 7.07 (br d, 1 H), 4.16 (q, 2 H), 3.67 (s, 2 H), 3.61 (s, 3 H), 2.06 (s, 3 H), 1.25 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 330 (M+NH<sub>4</sub>)<sup>+</sup>.



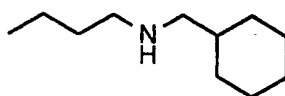
12720

#### Example 1140B

##### Methyl 4-(Carboxymethyl)-2-(2-methylphenyl)benzoate

To the solution of intermediate 1140A (213 mg, 0.682 mmol) in methanol (3 mL) was added NaOH (0.979 M in water, 0.697 mL). After 2 hours, the reaction mixture was acidified with HCl (1.0 M, 1 mL), and was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was used without further purification.

12725



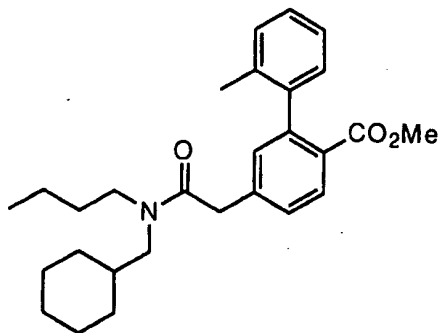
12730

#### Example 1140C

##### N-Butylcyclohexylmethanamine

The procedures described in the Example 1178E and 1178F were used here to convert cyclohexylacetyl chloride (1.47 g, 10.0 mmol) and butylamine to the title amine in 85% yield. The amine was not purified before it was used.

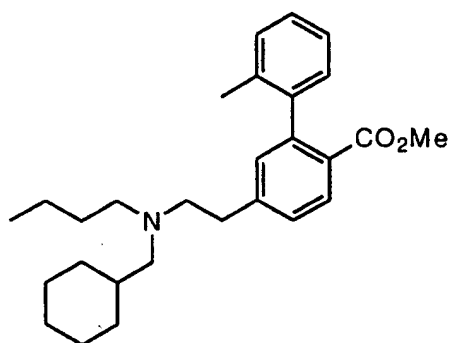
12735



#### Example 1140D

##### Methyl 4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoate

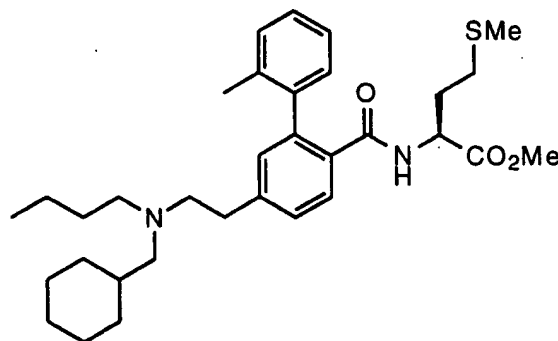
The procedure described in example 1144C was used here to combine intermediate 1140B (311 mg, 1.10 mmol) and intermediate 1140C (205 mg) to give the title compound (247 mg, 52%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.94 (d, 1 H), 7.33 (M, 1 H), 7.25-7.15 (m, 3 H), 7.13, 7.11 (2 d's, 1 H), 7.05 (m, 1 H), 3.76, 3.75 (2 s's, 2 H), 3.60 (s, 3 H), 3.35-3.05 (m, 4H), 2.05, 2.04 (2 s's, 3 H), 1.80-1.10 (m, 15 H), 0.91, 0.89 (2 t's, 3 H). MS(CI/NH<sub>3</sub>) m/z: 436 (M+H)<sup>+</sup>.



#### Example 1140E

##### Methyl 4(N-Cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoate

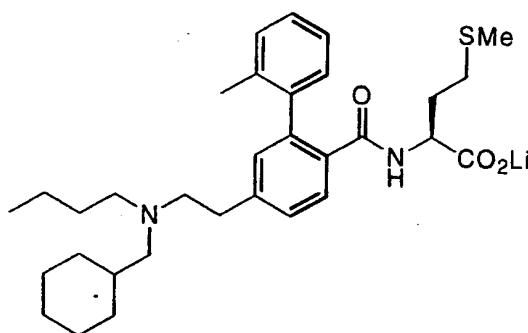
A solution of intermediate 1140D (118 mg, 0.271 mmol) and borane (1.0 M in THF, 0.54 mL) in THF was refluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. The it was cooled to room temperature, The reaction mixture was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the intermediate amine 1140E. The amine was used without further purification. <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (d, 1 H), 7.28-7.17 (m, 4 H), 7.05 (m, 2 H), 3.60 (s, 3 H), 2.75 (m, 2 H), 2.66 (m, 2 H), 2.40 (t, 2 H), 2.19 (d, 2 H), 2.06 (s, 3 H), 1.80-1.10 (m, 15 H), 0.88 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 422 (M+H)<sup>+</sup>.



Example 1140FN-[4-(N-Cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

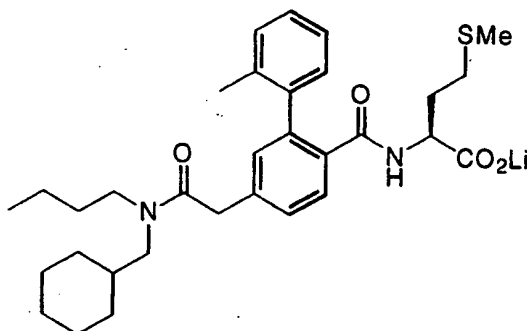
12765 The procedures described in the Example 403E and 403F were used here to convert the above intermediate amine 1140E to the title methyl ester (113 mg, 76%, 3 steps from 1140D). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (2 d's, 1 H), 7.34-7.18 (m, 5 H), 7.01 (s, 1 H), 5.87 (br d, 1 H), 4.62 (m, 1 H), 3.65 (s, 3 H), 2.75 (m, 2 H), 2.66 (m, 2 H), 2.41 (t, 2 H), 2.20 (d, 2 H), 2.19-1.98 (m, 8 H), 1.87 (m, 1 H), 1.80-1.10 (m, 16 H), 0.88 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 553 (M+H)<sup>+</sup>.

12770

Example 1140GN-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

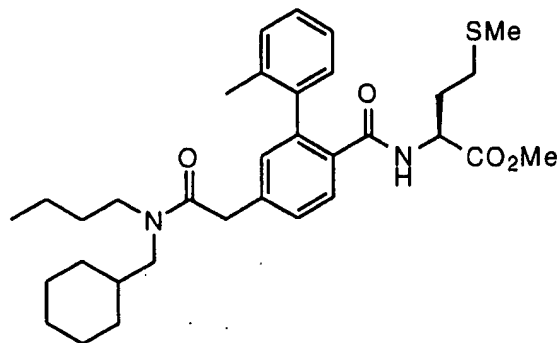
12775 The procedure described in the Example 403I was used here to convert the intermediate 1140F (107 mg) to the title lithium salt (91 mg, 87%). <sup>1</sup>H NMR (300 MHz, dmso-d<sub>6</sub>) δ 7.51 (d, 1 H), 7.33-7.13 (m, 5 H), 7.05 (br s, 1 H), 6.95 (m, 1 H), 3.71 (m, 1 H), 2.76 (m, 2 H), 2.67 (m, 2 H), 2.42 (t, 2 H), 2.21 (d, 2 H), 2.10-1.82 (m, 8 H), 1.80-1.10 (m, 17 H), 0.88 (t, 3 H). MS(ESI-) m/z: 537 (M-H)<sup>-</sup>.

12780

Example 1141

12785

N-[4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



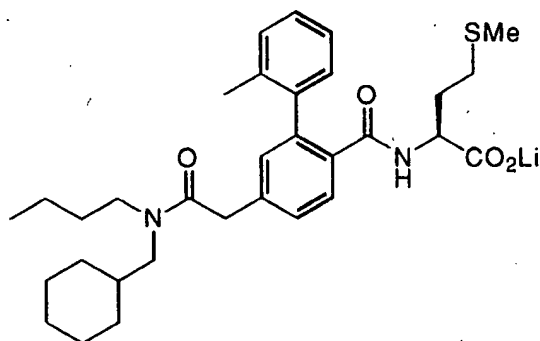
Example 1141A

12790

N-[4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedures described in the Example 403E and 403F were used here to convert the intermediate 1140D (101 mg) to the title methyl ester (127 mg, 97%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.92 (m, 1 H), 7.37-7.22 (m, 4 H), 7.19 (m, 1 H), 7.11 (br d, 1 H), 5.88 (br d, 1 H), 4.61 (m, 1 H), 3.76, 3.75 (2 s's, 2 H), 3.65 (s, 3 H), 3.37-2.04 (m, 4 H), 2.00-1.97 (m, 8 H), 1.95-1.10 (m, 17 H), 0.92, 0.88 (2 t's, 3 H). MS(CI/NH<sub>3</sub>) m/z: 567 (M+H)<sup>+</sup>.

12795



12800

Example 1141B

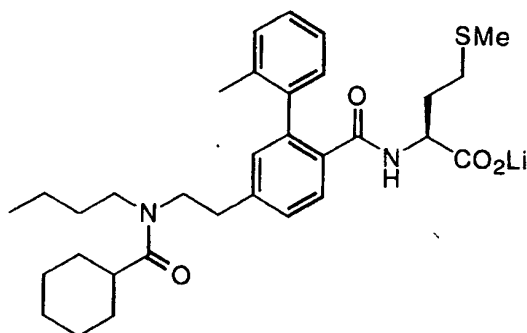
N-[4-(N-Cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1141A (119 mg) to the title lithium salt (102 mg, 86%). <sup>1</sup>H NMR (300 MHz, dms<sub>o</sub>-d<sub>6</sub>) δ 7.48 (2 d's, 1 H), 7.30 (m, 1 H), 7.25-7.08 (m, 4 H), 7.03 (br s, 1 H), 5.95 (m, 1 H), 3.74, 3.72 (2 s's, 2 H), 3.69 (m, 1 H), 3.23 (t, 2 H), 3.11 (m, 2 H), 2.20-1.90

12805

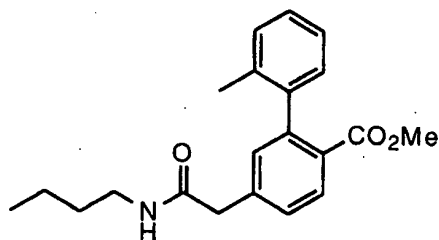
(m, 8 H), 1.85 (m, 1 H), , 1.79-1.00 (m, 17 H), 0.86,0.83 (2 t's, 3 H). MS(ESI-) m/z: 551 (M-H)<sup>-</sup>.

12810

Example 1142

N-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

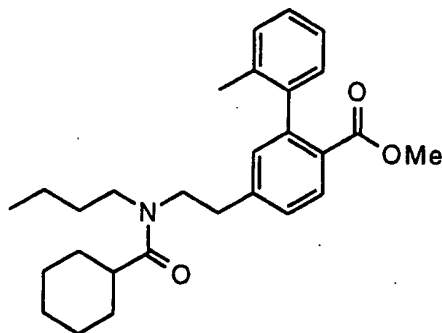
12815

Example 1142A

Methyl 4-(N-Butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoate

The procedure described in example 1144C was used here to combine intermediate

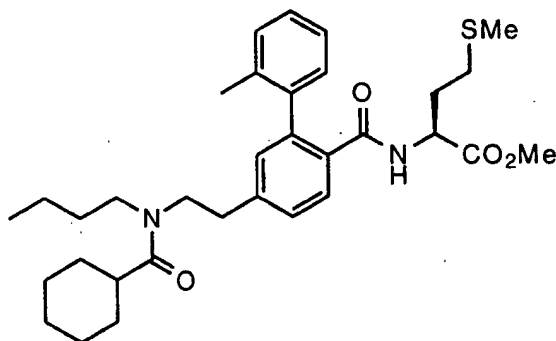
12820 1140B (200 mg, 0.70 mmol) and butylamine to give the title compound (171 mg, 69%).  
<sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.95 (d, 1 H), 7.34 (dd, 1 H), 7.30-7.17 (m, 3 H), 7.13 (d, 1 H), 7.05 (d, 1 H), 5.36 (m, 1 H), 3.61 (s, 3 H), 3.60 (s, 2 H), 3.24 (q, 1 H), 2.07 (s, 3 H), 1.42 (m, 2 H), 1.27 (m, 2 H), 0.88 (t, 3 H).



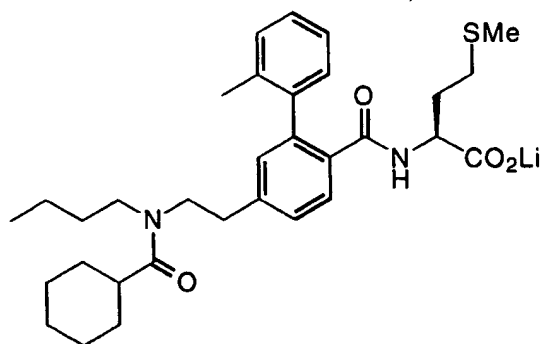
12825

Example 1142BMethyl N-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoate

The procedures described in 1143B was used here to convert 1142A (102 mg, 0.36 mmol) to the title compound (137 mg, 87%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.92 (2 d's, 1 H), 7.30-7.17 (m, 4 H), 7.05 (m, 2 H), 3.61 (2 s's, 3 H), 3.52 (m, 2 H), 3.07,3.06 (2 t's, 2 H), 2.90 (t, 2 H), 2.37 (m, 1 H), 2.07,2.04 (2s's, 3 H), 2.00-1.15 (m, 14 H), 0.92,0.90 (2 t's, 3 H). MS(CI/NH<sub>3</sub>) m/z: 436 (M+H)<sup>+</sup>.

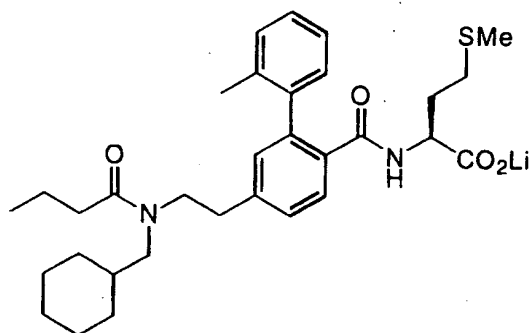
Example 1142CN-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedures described in the Example 403E and 403F were used here to convert the above intermediate 1142B (130 mg) to the title methyl ester (112 mg, 66%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.91 (2 d's, 1 H), 7.37-7.15 (m, 5 H), 7.06,6.99 (2 br s's, 1 H), 6.90 (br d, 1 H), 4.61 (m, 1 H), 3.66,2.65 (2 s's, 3 H), 3.52 (m, 2 H), 3.19,2.92 (2 m's, 4 H), 2.30-2.00 (m, 9 H), 1.86 (m, 1 H), 1.80,1.10 (m, 15 H), 0.94,0.91 (2 t's, 3 H). MS(CI/NH<sub>3</sub>) m/z: 567 (M+H)<sup>+</sup>.

Example 1142DN-[4-(N-Cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

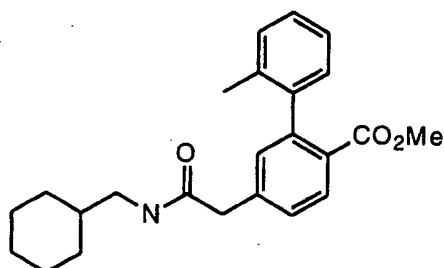
12850 The procedure described in the Example 403I was used here to convert the intermediate 1142C (103 mg) to the title lithium salt (99 mg, 97%).  $^1\text{H}$  NMR (300 MHz,  $\text{dmso-d}_6$ )  $\delta$  7.48 (2 d's, 1 H), 7.31-6.86 (m, 7 H), 3.63 (m, 1 H), 3.48 (m, 2 H), 3.10, 2.95 (2 m's, 2 H), 2.82 (2 t's, 2 H), 2.25-1.90 (m, 9 H), 1.80 (m, 1 H), 1.75-1.07 (m, 15 H), 0.84, 0.80 (2 t's, 3 H). MS(ESI-)  $m/z$ : 551 ( $\text{M-H}$ ) $^-$ .

12855

Example 1143

N-[4-(N-Cyclohexylmethyl)-N-butanoylaminoethyl]-2-(2-methylphenyl)benzoyl]methionine  
lithium salt

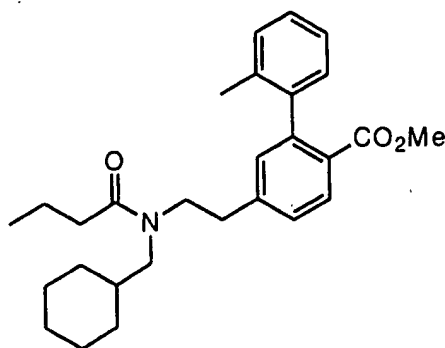
12860

Example 1143A

Methyl 4-(N-Cyclohexylmethylaminocarbonylmethyl)-2-(2-methylphenyl)benzoate

12865 The procedure described in example 1144C was used here to combine intermediate 1140B (301 mg, 1.05 mmol) and cyclohexylmethylamine to give the title compound (266 mg, 67%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (d, 1 H), 7.35 (dd, 1 H), 7.27-7.17 (m, 3 H), 7.15 (d, 1 H), 7.05 (d, 1 H), 5.41 (m, 1 H), 3.62 (2 overlapped s's, 5 H), 3.07 (t, 2 H), 2.06 (s, 3 H), 1.85-0.87 (m, 11 H). MS( $\text{CI}/\text{NH}_3$ )  $m/z$ : 380 ( $\text{M}+\text{H}$ ) $^+$ .

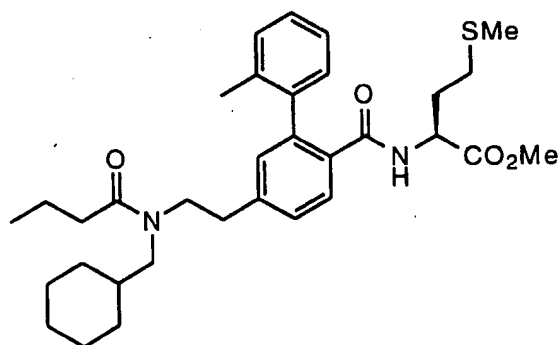




### Example 1143B

#### Methyl 4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoate

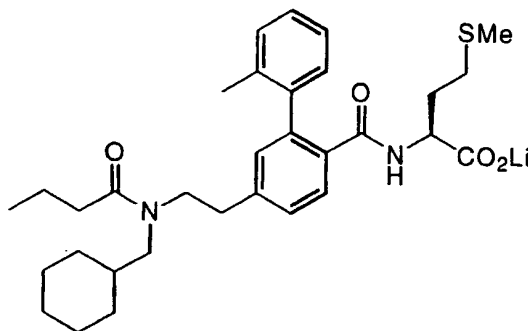
To a solution of intermediate 1143A (108 mg, 0.285 mmol) in THF (2 mL) was added borane (1.0 M in THF, 0.5 mL), and the reaction mixture was stirred at room temperature for 7 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. Then it was cooled to room temperature, and was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). While still in the separatory funnel, butyryl chloride (0.5 mL) was added to the organic layer, followed by additon of sodium bicarbonate (saturated in water, 5 mL), and the mixture was well shaken. The mixture was washed with NaOH (1.0 M, 10 mL), water (2 X 10 mL), brine (10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 20% ethyl acetate in hexane to give the title compound ( to give the title amine (113 mg, 91%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.94 (2d'd, 1 H), 7.31-7.18 (m, 4 H), 7.10-7.02 (m, 2 H), 3.62,3.61 (2 s's, 3 H), 3.52 (m, 2 H), 3.00-2.85 (m, 4 H), 2.26,2.18 (2 t's, 2 H), 2.06,2.05 (2 s's, 3 H), 1.80-0.80 (m, 13 H), 0.94,0.91 (2 t's, 3 H). MS(CI/NH<sub>3</sub>) m/z: 436 (M+H)<sup>+</sup>.



### Example 1143C

#### N-[4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

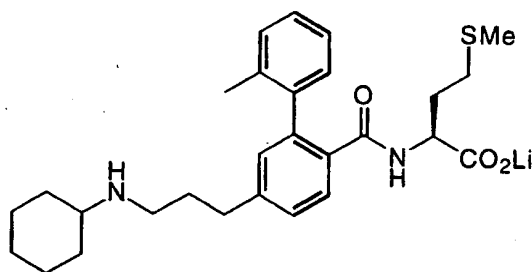
The procedures described in the Example 403E and 403F were used here to convert the above intermediate 1143B (130 mg, 0.300 mmol) to the title methyl ester (112 mg, 66%).  $^1\text{H}$ NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (m, 1 H), 7.35-7.21 (m, 4 H), 7.19 (m, 1 H), 7.03 (br d, 1 H), 5.89 (br d, 1 H), 4.61 (m, 1 H), 3.65 (s, 3 H), 3.52 (m, 2 H), 3.30, 3.07 (2 m's, 2 H), 2.90 (t, 2 H), 2.40-1.97 (m, 10 H), 1.90-1.10 (m, 15 H), 0.92, 0.90 (2 t's, 3 H). MS( $\text{CI}/\text{NH}_3$ )  $m/z$ : 567 ( $\text{M}+\text{H}$ ) $^+$ .



#### Example 1143D

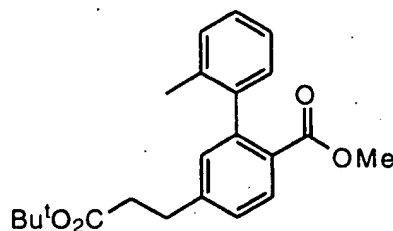
N-[4-(N-Cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1143C (104 mg) to the title lithium salt (95 mg, 100%).  $^1\text{H}$  NMR (300 MHz,  $\text{dms}\text{-}d_6$ )  $\delta$  7.48 (2 d's, 1 H), 7.31-7.10 (m, 5 H), 7.10-6.87 (m, 2 H), 3.66 (m, 1 H), 3.57-3.39 (m, 2 H), 3.22, 3.09 (2 m's, 2 H), 2.85, 2.79 (2 t's, 2 H), 2.40, 2.25 (2 m's, 2 H), 2.20-1.90 (m, 8 H), 1.83 (m, 1 H), 1.75-1.06 (m, 14 H), 0.87, 0.85 (2 t's, 3 H). MS(ESI $^-$ )  $m/z$ : 551 ( $\text{M}-\text{H}$ ) $^-$ .



#### Example 1144

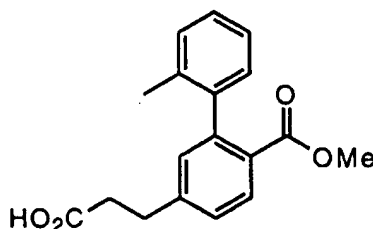
N-[4-(N-Cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1144AMethyl 4-(tert-Butoxycarbonylethyl)-2-(2-methylphenyl)benzoate

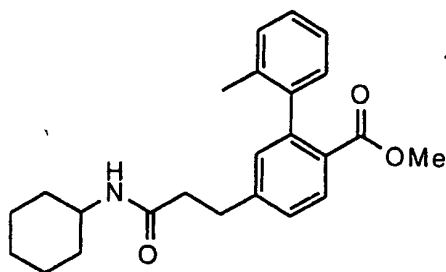
To a solution of (t-butoxycarbonylmethyl)triphenylphosphonium bromide (10.98 g, 24.0 mmol) in THF (150 mL) at 0 °C was added potassium t-butoxide (1.0 M in THF, 24 mL) over 5 min. After 2 h, the aldehyde from example 1171A (20 mmol) in THF (10 mL) was added slowly over 5 min., and the reaction was further stirred for 30 min. The reaction mixture was diluted with hexane (200 mL), and the resulting muddy mixture was filtered through silica gel (200 g), rinsed with ether, and concentrated to give an intermediate olefin.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.97 (d, 1 H), 7.59 (d, 1 H), 7.54 (dd, 1 H), 7.37 (d, 1 H), 7.30-7.27 (m, 3 H), 7.06 (d, 1 H), 6.44 (d, 1 H), 3.61 (s, 3 H), 2.06 (s, 3 H), 1.52 (s, 9 H). MS(CI/NH<sub>3</sub>) m/z: 353 (M+H)<sup>+</sup>, 370 (M+NH<sub>4</sub>)<sup>+</sup>.

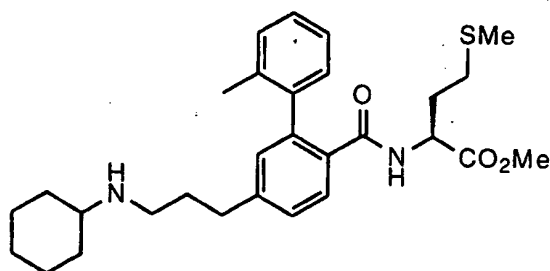
That intermediate was mixed with palladium on carbon (10%, 2.0 g) in ethanol (30 mL), and was stirred under a hydrogen balloon overnight. The mixture was then filtered through Celite<sup>TM</sup> (5 g), and the filtrate was concentrated. The residue was then redissolved in ether (100 mL) and the solution was filtered through silica gel (30 g). Concentration of the filtrate afforded the title compound (7.27 g, 99% for 2 steps). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.91 (d, 1H), 7.28-7.15 (m, 4 H), 7.07-7.03 (m, 2 H), 3.60 (s, 3 H), 2.97 (t, 2 H), 2.57 (t, 2 H), 2.05 (s, 3 H), 1.40 (s, 9 H). MS(CI/NH<sub>3</sub>) m/z: 355 (M+H)<sup>+</sup>, 372 (M+NH<sub>4</sub>)<sup>+</sup>.

Example 1144BMethyl 4-(2-Carboxyethyl)-2-(2-methylphenyl)benzoate

A solution of intermediate 1144A (5.00 g) in trifluoroacetic acid (20 mL) and methyl sulfide (3 mL) was stirred at room temperature for 7 hours. Solvent was then evaporated to give an off-white solid, which was used without further purification.

Example 1144C12945 Methyl 4-(2-Cyclohexylcarbomoyl)ethyl-2-(2-methylphenyl)benzoate

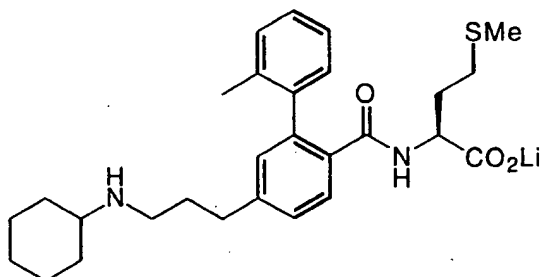
To a solution of intermediate 1144B (150 mg, 0.50 mmol), oxalyl chloride (2.0 M in DCM, 0.5 mL) in DCM (2 mL) was added a small drop of DMF. After 2 hours at room temperature, the reaction was concentrated to dryness, and redissolved in DCM (3 mL). To it was added cyclohexylamine (99 mg, 1 mmol) and triethylamine (100 mg, 1 mmol). After 15 min., HCl (1.0 M in ether, 2.0 mL) was added to the reaction mixture, and it was filtered through silica gel (5 g). The residue after concentration of the filtrate was purified by column chromatography with 20% ethyl acetate in hexane to give the title compound (152 mg, 80%).  
 12950 <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (d, 1 H), 7.28-7.15 (m, 4 H), 7.07-7.02 (m, 2 H), 5.16 (m, 1 H), 3.72 (m, 1 H), 3.60 (s, 3H), 3.02 (t, 2 H), 2.45 (t, 2 H), 2.05 (s, 3 H), 1.85 (m, 2 H), 1.70-1.55 (m, 3 H), 1.40-0.95 (m, 6 H). MS(Cl/NH<sub>3</sub>) m/z: 380 (M+H)<sup>+</sup>, 397 (M+NH<sub>4</sub>)<sup>+</sup>.  
 12955

Example 1144D12960 N-[4-(N-Cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine

A solution of intermediate 1144C (150 mg, 0.40 mmol) and borane (1.0 M in THF, 1.0 mL) in THF (1 mL) was refluxed for 15 hours. Methanol (0.5 mL) was added dropwisly to the reaction, followed by concentrated HCl (0.5 mL), and the mixture was heated at 60 °C for 1 hour. The reaction mixture was cooled to room temperature, and was adjusted to pH about 12-14 with sodium carbonate (2.0 M in water). The reaction mixture was then  
 12965 partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and

concentrated to give the intermediate amine. The amine was used without further purification. MS(CI/NH<sub>3</sub>) m/z: 366 (M+H)<sup>+</sup>.

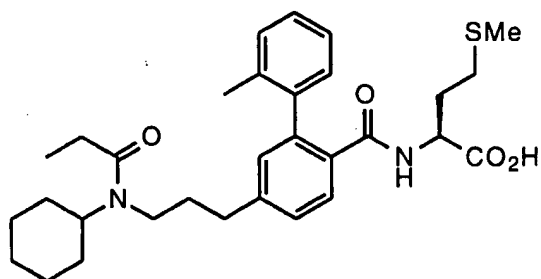
12970 The procedures described in the Example 403E and 403F were used here to convert the above intermediate amine to the title methyl ester (58%, 3 steps).



#### Example 1144E

12975 N-[4-(N-Cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1144D (121 mg) to the title lithium salt (107 mg, 100%). <sup>1</sup>H NMR (300 MHz, dmso-d<sub>6</sub>) δ 7.45 (d, 1 H), 7.27-7.08 (m, 4 H), 7.02-6.93 (m, 2 H), 6.90 (m, 1 H), 3.80 (m, 1 H), 3.65 (m, 1 H), 3.30 (m, 2 H), 2.64 (t, 2 H), 2.20-1.80 (m, 10 H), 1.80-1.45 (m, 7 H), 1.30-0.88 (m, 6 H). MS(ESI-) m/z: 481 (M-H)<sup>-</sup>.



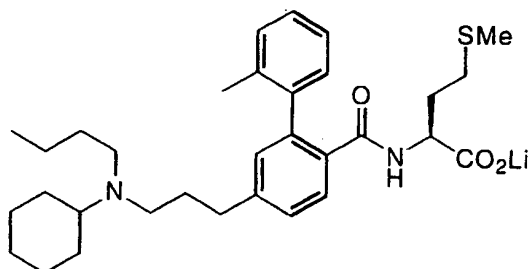
#### Example 1145

12985 N-[4-(N-Cyclohexyl-N-propanoylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine

To a stirred mixture of 1144E (70 mg, 0.14 mmol) in THF (1 mL) and saturated aqueous sodium bicarbonate (1 mL) was added propionyl chloride (0.10 mL). After 10 min, the reaction mixture was adjusted to pH 4-5, and it was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (10 mL), brine (10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was heated at 60 °C under high vacuum for 5 hours to give the title compound (59 mg, 78%). <sup>1</sup>H NMR (300 MHz, dmso-d<sub>6</sub>) δ 7.47 (m, 1 H), 7.32-6.97 (m, 7 H), 4.25 (m, 1 H),

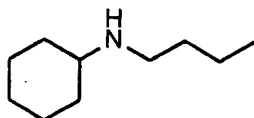
3.57 (m, 1 H), 3.35 (m, 2 H), 2.80-2.60 (m, 2 H), 2.30-1.85 (m, 12 H), 1.85-1.45 (m, 7 H), 1.30-0.88 (m, 9 H). MS(ESI-) m/z: 537 (M-H)<sup>-</sup>.

12995

Example 1146

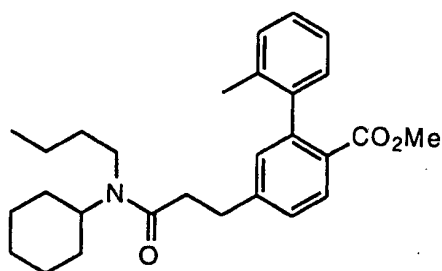
N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

13000

Example 1146AN-Butylcyclohexylamine

13005

The procedures described in the Example 1178E and 1178F were used here to convert butyric chloride and cyclohexylamine to the title amine in 86% yield. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.62 (t, 2 H), 2.41 (m, 1 H), 1.95-1.00 (m, 15 H), 0.92 (t, 3 H). MS(Cl/NH<sub>3</sub>) m/z: 156 (M+H)<sup>+</sup>.



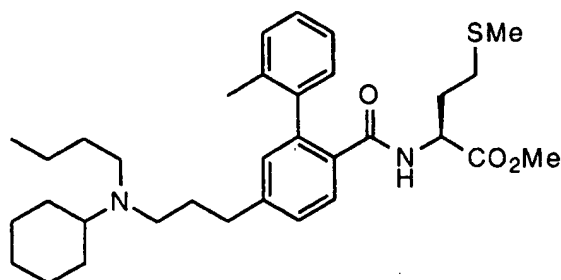
13010

Example 1146BMethyl N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoate

13015

The procedure described in the Example 1144C was used here to convert the intermediate 1144B (298 mg) and N-butylcyclohexylamine (intermediate 1146A, 310 mg, 2.0 mmol) to the title methyl ester (233 mg, 54%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (2 d's, 1 H), 7.30-7.15 (m, 4 H), 7.07 (m, 2 H), 4.25 (m, 1 H), 3.60 (s, 3 H), 3.18 (m, 1

H), 3.05 (m, 3 H), 2.62 (m, 2 H), 2.06 (2s's, 3 H), 1.85-1.05 (m, 14 H), 0.90 (2 t's, 3 H). MS(CI/NH<sub>3</sub>) m/z: 436 (M+H)<sup>+</sup>.



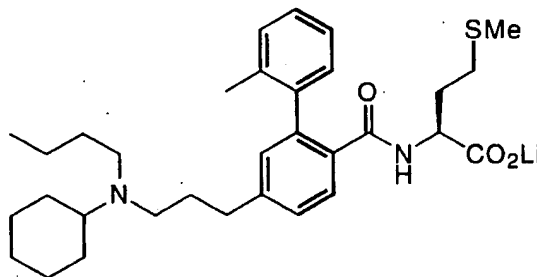
13020

#### Example 1146C

#### N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedure described in the Example 1144C was used here to convert the intermediate 1146B (230 mg) to the title methyl ester (184 mg, 63%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (2 d's, 1 H), 7.35-7.19 (m, 4 H), 7.03 (m, 1 H), 5.89 (m, 1 H), 4.62 (m, 1 H), 3.66 (s, 3 H), 3.05 (m, 1 H), 2.66 (t, 2 H), 2.46 (t, 2 H), 2.41 (t, 2 H), 2.20-2.00 (4 s's, 6 H), 2.05 (m, 2 H), 1.90-1.00 (m, 18 H), 0.90 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 553 (M+H)<sup>+</sup>.

13030

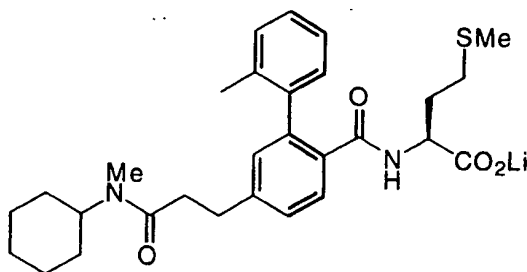


#### Example 1146D

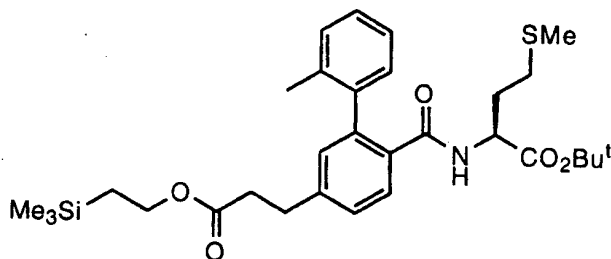
#### N-[4-(N-Cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1146C (179 mg) to the title lithium salt (153 mg, 81%). <sup>1</sup>H NMR (300 MHz, dmsO-d<sub>6</sub>) δ 7.46 (m, 1 H), 7.35-7.08 (m, 4 H), 7.07-6.90 (m, 2 H), 3.70 (m, 1 H), 3.05 (m, 1 H), 2.64 (t, 2 H), 2.37 (m, 4 H), 2.20-1.90 (m, 8 H), 1.90-0.95 (m, 18 H), 0.85 (t, 3 H). MS(ESI-) m/z: 537 (M-H)<sup>-</sup>.

13040

Example 1147

N-[4-(N-Cyclohexyl-N-methylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine  
lithium salt

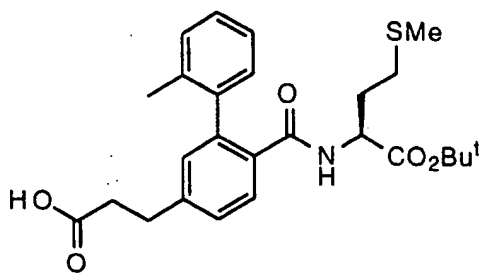
Example 1147A

[4-(2-Trimethylsilylethoxycarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine tert-Butyl  
Ester

A solution of intermediate 1144A (875 mg, 2.38 mmol) and LiOH (5.3 M in water, 2.0 mL) in methanol (5 mL) was refluxed 15 hours. The mixture was then acidified with concentrated HCl (1 mL) to pH<3. The reaction mixture was then partitioned between ethyl acetate (100 mL) and brine (20 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated. The resulting white solid was desolved in DMF (10 mL). To it was added 2-trimethylsilylethanol (0.357 mL, 2.49 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (545 mg, 2.84 mmol), and DMAP (10 mg). After 2 hours, triethylamine (809 mg, 8.0 mmol) L-methionine tert-butyl ester hydrochloride (725 mg, 3.0 mmol), 1-hydroxybenzotriazole (400 mg, 3.0 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (577 mg, 3.0 mmol). After 15 hours at room temperature, the reaction mixture was partitioned between ethyl acetate (100 mL) and water (10 mL). The organic layer was washed with water (3 X 15 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 10% ethyl acetate in hexane to give the title compound (859 mg, 68%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.83 (2 d'd, 1 H), 7.33-7.15 (m, 5 H), 7.04 (br s, 1 H), 5.85 (br d, 1 H), 4.50 (m, 1 H), 4.16 (t, 2 H), 3.00 (t, 2 H), 2.63 (t, 2 H),



2.17, 2.07, 2.03, 2.02 (4 s's, 6 H), 2.00 (m, 2 H), 1.80 (m, 1 H), 1.55 (m, 1 H), 1.40 (s, 9 H), 0.95 (t, 2 H), 0.03 (s, 9 H). MS(CI/NH<sub>3</sub>) m/z: 572 (M+H)<sup>+</sup>.



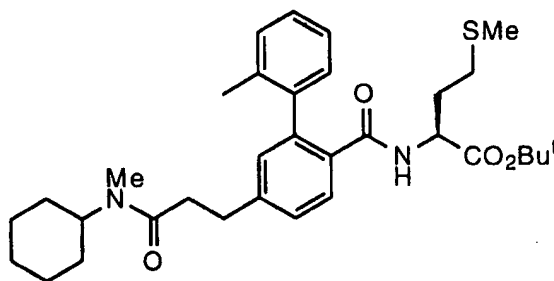
13070

#### Example 1147B

##### [4-(2-Carboxyethyl)-2-(2-methylphenyl)benzoyl]methionine tert-Butyl Ester

A solution of intermediate 1147A (841 mg, 1.57 mmol), tetrabutylammonium fluoride (820 mg, 3.14 mmol) in DMF (5 mL) was stirred overnight. The reaction mixture was then adjusted to pH 3-5, and was partitioned between ethyl acetate (100 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to give the title compound. The crude product was used without further purification. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.83 (2 d'd, 1 H), 7.33-7.15 (m, 5 H), 7.05 (br s, 1 H), 5.87 (m, 1 H), 4.50 (m, 1 H), 3.01 (t, 2 H), 2.71 (t, 2 H), 2.20-2.02 (4 s's, 6 H), 2.00 (m, 2 H), 1.80 (m, 1 H), 1.59 (m, 1 H), 1.40 (s, 9 H). MS(CI/NH<sub>3</sub>) m/z: 472 (M+H)<sup>+</sup>.

13080



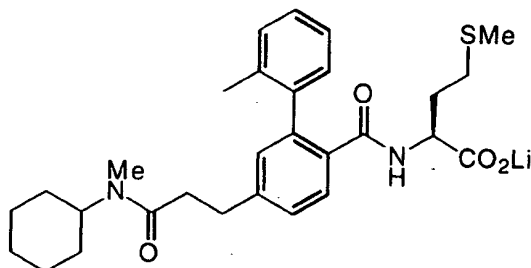
#### Example 1147C

##### N-[4-(N-Cyclohexyl-N-methylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine tert-Butyl Ester

A solution of intermediate 1147B (50 mg, 0.115 mmol), triethylamine (100 mg), 1-hydroxybenzotriazole (31 mg, 0.23 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (44 mg, 0.23 mmol), and N-methylcyclohexylamine (26 mg, 0.23 mmol) in DMF (2 mL) was stirred 15 hours at room temperature. The reaction mixture was then partitioned between ethyl acetate (50 mL) and water (5 mL). The organic layer was washed with water (3 X 5 mL), brine (5 mL), dried over anhydrous magnesium sulfate, filtered and

13090

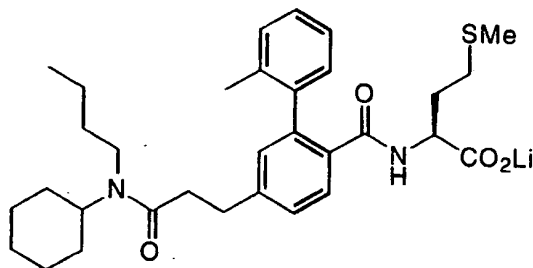
concentrated. The residue was purified by column chromatography with 40% ethyl acetate in hexane to give the title compound (44 mg, 68%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.84 (m, 1 H), 7.33-7.15 (m, 5 H), 7.05 (br s, 1 H), 5.84 (m, 1 H), 4.47 (m, 2 H), 3.02 (t, 2 H), 2.81, 2.77 (2s's, 3 H), 2.62 (m, 2 H), 2.20-1.97 (m, 8 H), 1.90-1.25 (m, 12 H), 1.40 (s, 9 H). MS(CI/ $\text{NH}_3$ )  $m/z$ : 567 ( $\text{M}+\text{H}$ ) $^+$ .



#### Example 1147D

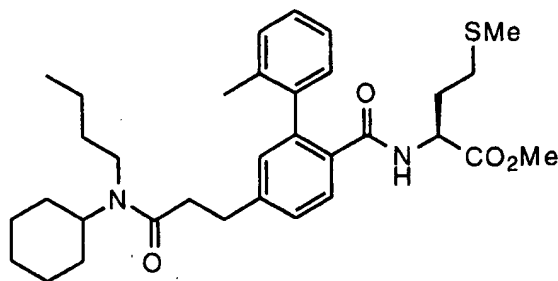
#### N-[4-(N-Cyclohexyl-N-methylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

The intermediate 1147C (40 mg) was stirred with HCl (4.0  $\text{N}$  in dioxane, 1.0 mL) in DCM (1 mL) at room temperature for 15 hours. Solvent was then evaporated, and the residue was desolved in acetonitrile (1 mL), treated with 1.1 equivalent of LiOH (1.0  $\text{M}$  in water, 0.078 mL), and freeze-dried to give the title compound (37 mg, 100%).  $^1\text{H}$  NMR (300 MHz,  $\text{dmso}-d_6$ )  $\delta$  7.44 (d, 1 H), 7.30 (m, 1 H), 7.25-7.08 (m, 4 H), 7.03 (m, 1 H), 6.87 (m, 1 H), 4.23 (m, 1 H), 3.66 (m, 1 H), 2.87 (m, 2 H), 2.74, 2.66 (2s's, 3 H), 2.62 (m, 2 H), 2.20-1.90 (m, 8 H), 1.90-1.25 (m, 12 H). MS(ESI-)  $m/z$ : 509 ( $\text{M}-\text{H}$ ) $^-$ .

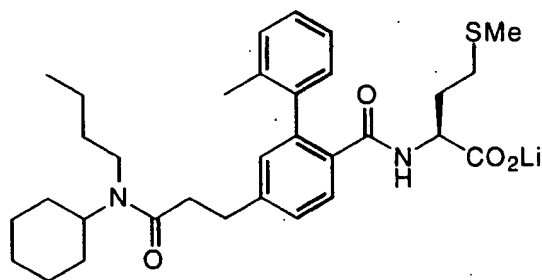


#### Example 1148

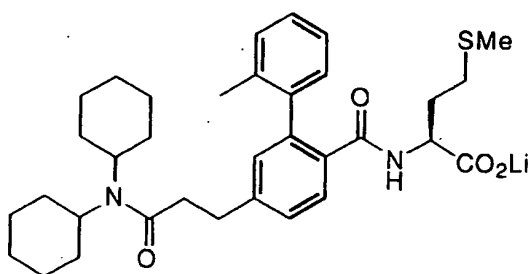
#### N-[4-(N-Cyclohexyl-N-butylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1148AN-[4-(N-Cyclohexyl-N-butylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionineMethyl ester

The procedures described in the Example 403E and 403F were used here to convert the intermediate 1146B (102mg) to the title methyl ester (117 mg, 90%). <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 7.91 (2 d's, 1 H), 7.35-7.15 (m, 5 H), 7.06 (br s, 1 H), 6.88 (m, 1 H), 4.61 (m, 1 H); 3.49 (m, 1 H), 3.66 (s, 3 H), 3.20-3.00 (m, 4 H), 2.66-2.50 (m, 2 H), 2.20-2.00 (m, 8 H), 1.90-0.95 (m, 16 H), 0.91 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 566 (M+H)<sup>+</sup>.

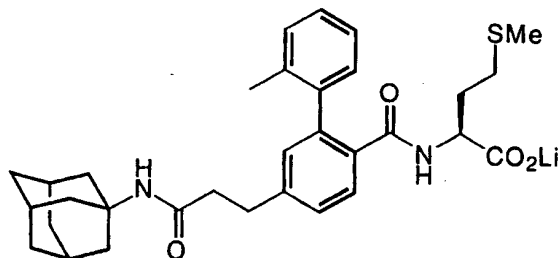
Example 1148BN-[4-(N-Cyclohexyl-N-butylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methioninelithium salt

The procedure described in the Example 403I was used here to convert the intermediate 1148A (108 mg) to the title lithium salt (91 mg, 83%). <sup>1</sup>HNMR (300 MHz, dmso-d<sub>6</sub>) δ 7.44 (d, 1 H), 7.27 (t, 1 H), 7.23-7.05 (m, 3 H), 7.04-6.91 (m, 2 H), 6.89 (d, 1 H), 4.07 (m, 1 H), 3.65 (m, 1 H), 3.06 (m, 2 H), 2.88 (m, 2 H), 2.65, 2.57 (2 t's, 2 H), 2.20-1.90 (m, 8 H), 1.90-0.95 (m, 16 H), 0.84 (t, 3 H). MS(ESI-) m/z: 537 (M-H)<sup>-</sup>.

Example 1149

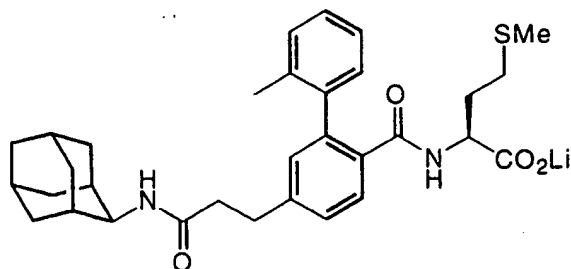
13140 N-[4-(N,N-dicyclohexylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

The procedures described in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (30 mg, 45%, 2 steps). <sup>1</sup>HNMR (300 MHz, dmso-d<sub>6</sub>) δ 7.44 (d, 1 H), 7.30 (m, 1 H), 7.25-7.08 (m, 4 H), 7.03 (m, 1 H), 6.87 (m, 1 H), 4.18 (m, 1 H), 3.66 (m, 1 H), 2.87 (t, 2 H), 2.60 (t, 2 H), 2.20-1.90 (m, 8 H), 1.75-1.00 (m, 22 H). MS(ESI-) m/z: 577 (M-H)<sup>-</sup>.

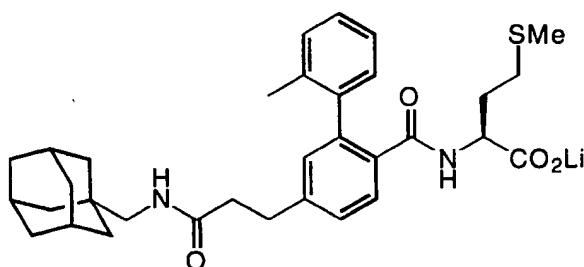
Example 1150

13150 N-[4-(N-adamant-1-ylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

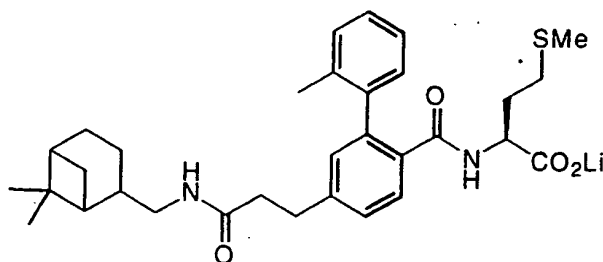
The procedures described in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (40 mg, 62%, 2 steps). <sup>1</sup>HNMR (300 MHz, dmso-d<sub>6</sub>) δ 7.63 (d, 1 H), 7.44 (d, 1 H), 7.27-7.05 (m, 5 H), 6.98 (m, 1 H), 6.88 (m, 1 H), 3.80 (m, 1 H), 3.64 (m, 1 H), 2.87 (m, 2 H), 2.50 (m, 2 H), 2.20-1.80 (m, 17 H), 1.77-1.45 (m, 8 H). MS(ESI-) m/z: 547 (M-H)<sup>-</sup>.

**Example 1151****N-[4-(N-adamant-2-ylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt**

The procedures described in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (41 mg, 64%, 2 steps). <sup>1</sup>HNMR (300 MHz, dms<sub>o</sub>-d<sub>6</sub>) δ 7.44 (m, 1 H), 7.30-7.05 (m, 6 H), 7.00 (m, 1 H), 6.88 (m, 1 H), 3.67 (m, 1 H), 2.82 (m, 2 H), 2.35 (m, 2 H), 2.20 -1.45 (m, 25 H). MS(ESI-) m/z: 547 (M-H)<sup>-</sup>.

**Example 1154****N-[4-(N-adamant-1-ylmethylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt**

The procedures described in the Example 1147C and 1147D were used here to convert 1147B (50 mg) to the title lithium salt (47 mg, 72%, 2 steps). <sup>1</sup>HNMR (300 MHz, dms<sub>o</sub>-d<sub>6</sub>) δ 7.61 (t, 1 H), 7.44 (d, 1 H), 7.25 (dd, 1 H), 7.24-7.08 (m, 4 H), 6.99 (br s, 1 H), 6.88 (m, 1 H), 3.62 (m, 1 H), 2.82 (t, 2 H), 2.73 (d, 2 H), 2.45 (t, 2 H), 2.20-1.90 (m, 8 H), 1.75-1.48 (m, 11 H), 1.35 (d, 6 H). MS(ESI-) m/z: 561 (M-H)<sup>-</sup>.

Example 1155

N-[4-(N-Mytanylmethylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

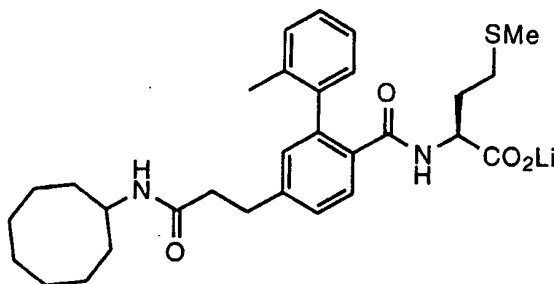
13185

The procedures described in the Example 1147C and 1147D were used here to

convert 1147B (50 mg) to the title lithium salt (45 mg, 70%, 2 steps). <sup>1</sup>H NMR (300 MHz, dms<sub>o</sub>-d<sub>6</sub>) δ 7.60 (t, 1 H), 7.44 (d, 1 H), 7.28-7.08 (m, 5 H), 6.99 (br s, 1 H), 6.88 (m, 1 H), 3.66 (m, 1 H), 3.00 (m, 2 H), 2.83 (t, 2 H), 2.39 (t, 2 H), 2.33-1.20 (m, 19 H), 1.13

13190

(s, 3 H), 0.97 (s, 3 H). MS(ESI<sup>-</sup>) m/z: 549 (M-H)<sup>-</sup>.

Example 1157

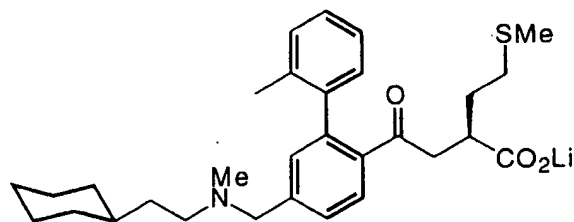
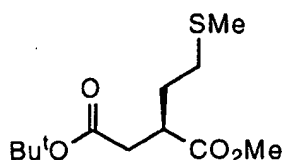
N-[4-(N-Cyclooctanylaminocarbonyl)ethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

13195

The procedures described in the Example 1147C and 1147D were used here to

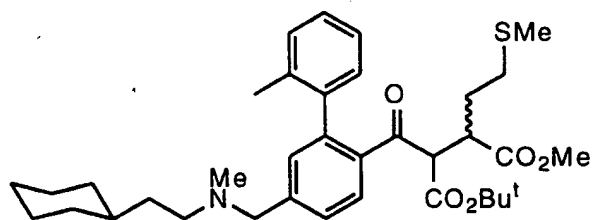
convert 1147B (50 mg) to the title lithium salt (31 mg, 51%, 2 steps). <sup>1</sup>H NMR (300 MHz, dms<sub>o</sub>-d<sub>6</sub>) δ 7.67 (d, 1 H), 7.44 (d, 1 H), 7.25-7.08 (m, 5 H), 6.96 (br s, 1 H), 6.88 (m, 1 H), 3.72 (m, 1 H), 3.63 (m, 1 H), 2.85 (t, 2 H), 2.36 (t, 2 H), 2.20-1.90 (m, 8 H), 1.90-1.30 (m, 16 H). MS(ESI<sup>-</sup>) m/z: 523 (M-H)<sup>-</sup>.

13200

Example 1158Example 1158AMethyl 2-(tert-butoxycarbonylmethyl)-4-methylthiobutyrate

To a -78 °C solution of methyl 4-methylthiobutyrate (1.48 g, 10.0 mmol) in THF (20 mL) was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 11 mL). After 30 min, tert-butyl bromoacetate (2.34 g, 12.0 mmol) was added to the reaction, and the reaction mixture was gradually warmed to the room temperature over 6 hours. The reaction mixture was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with water (2 X 20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 5% ethyl acetate in hexane to give the title compound (1.21 g, 46%).

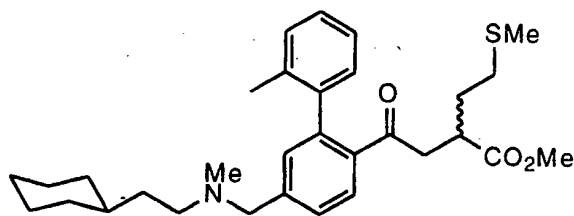
<sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ 3.75 (s, 3 H), 2.71 (t, 2 H), 2.51 (t, 2 H), 2.32 (m, 1 H), 2.06 (s, 1 H), 1.89 (t, 1 H), 1.41 (s, 9 H). MS(CI/NH<sub>3</sub>) m/z: 263 (M+H)<sup>+</sup>.

Example 1158B

To a solution of the acid from example 608C (530 mg, 1.32 mmol) in DCM (2 mL) was added oxalyl chloride (2.0 M in DCM, 1.5 mL), followed by a small drop of DMF.

After 2 hours at room temperature, the solvent was removed, and the residue was further dried under high vacuum (1 mmHg) for 1 hour. The solid (acid chloride) was redissolved in THF (5 mL).

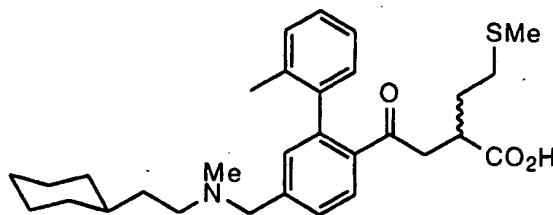
To a  $-78^{\circ}\text{C}$  solution of 1158A (1.21 g, 4.61 mmol) in THF (10 mL) in a separate flask was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 5.28 mL). After 30 min., the acid chloride solution was added slowly to the reaction mixture via a cannula. After 1 hour, the reaction mixture was quenched with saturated aqueous ammonium chloride (3 mL) at  $-78^{\circ}\text{C}$ . After it reached the room temperature, the reaction mixture was then partitioned between ethyl acetate (80 mL) and water (20 mL). The organic layer was washed with sodium bicarbonate (saturated in water, 10 mL), water (2 X 10 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 30% ethyl acetate in hexane to give the title compound (430 mg, 53%).  $^1\text{H}$ NMR is messy because of 4 diastereomers exist. MS( $\text{Cl}/\text{NH}_3$ )  $m/z$ : 610 ( $\text{M}+\text{H}$ ) $^+$ .



Example 1158C

Methyl 3-[4-(N-cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-4-methylthiobutyrate

A solution of 1158B (420 mg, 0.69 mmol) in HCl (4.0 M in 1,4-dioxane, 5 mL) was heated at  $80^{\circ}\text{C}$  for 2 hours. Solvent was evaporated, and the residue was redissolved in ethyl acetate (100 mL). The mixture was then washed with sodium bicarbonate (saturated in water, 20 mL), water (20 mL), brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography with 30% ethyl acetate in hexane to give the title compound (121 mg, 34%).  $^1\text{H}$ NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 (d, 1 H), 7.40 (br d, 1 H), 7.31-7.12 (m, 4 H), 7.07 (br d, 1 H), 3.62 (s, 3 H), 3.54 (br s, 2 H), 2.85 (m, 1 H), 2.71 (m, 1 H), 2.40 (m, 2 H), 2.35-2.00 (m, 12 H), 1.80-0.80 (m, 15 H). MS( $\text{Cl}/\text{NH}_3$ )  $m/z$ : 510 ( $\text{M}+\text{H}$ ) $^+$ .



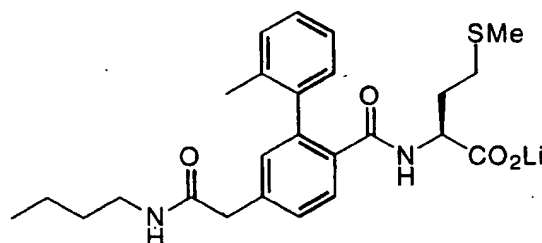
Example 1158D



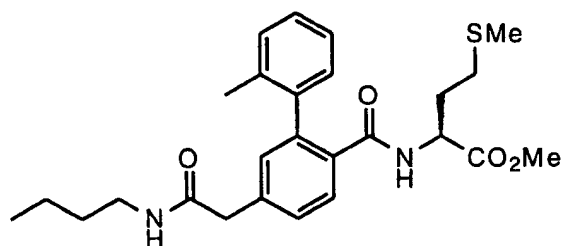
3-[4-(N-Cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-4-methylthiobutyric acid

The intermediate 1158C (112 mg) in MeOH (2 mL) and lithium hydroxide (1.0 M in water, 0.7 mL) was heated at 50 °C for 5 hours. The reaction mixture was then adjusted to pH 4-5 with KH<sub>2</sub>PO<sub>4</sub> (saturated in water), and extracted with ethyl acetate (3 X 20 mL).

The combined extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated to give the title compound (110 mg, 100%). <sup>1</sup>H NMR (300 MHz, dmsO-d<sub>6</sub>) δ 7.77 (m, 1 H), 7.61 (br d, 1 H), 7.40 (m, 1 H), 7.35-7.15 (m, 3 H), 7.07 (m, 1 H), 4.15 (br loop, 2 H), 2.88 (m, 2 H), 2.69 (m, 1 H), 2.28 (m, 2 H), 2.22-1.96 (m, 11 H), 1.72-0.80 (m, 15 H). MS(ESI-) m/z: 494 (M-H)<sup>-</sup>.



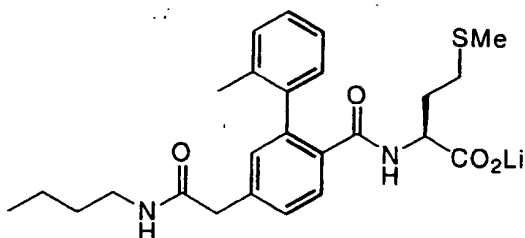
Example 1159



Example 1159A

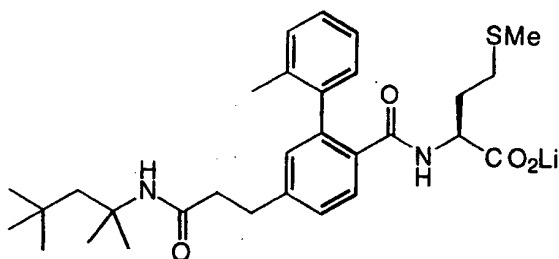
N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoylmethionine] lithium salt

The procedures described in the Example 403E and 403F were used here to convert intermediate 1142A (61 mg, 0.18 mmol) to the title methyl ester (70 mg, 83%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.95 (2 d's, 1 H), 7.39-7.15 (m, 5 H), 7.12 (br s, 1 H), 5.91 (br d, 1 H), 5.35 (m, 1 H), 4.63 (m, 1 H), 3.67 (s, 3 H), 3.61 (s, 2 H), 3.24 (q, 1 H), 2.20-1.99 (m, 8 H), 1.85 (m, 1 H), 1.60 (m, 1 H), 1.42 (m, 2 H), 1.27 (m, 2 H), 0.88 (t, 3 H). MS(CI/NH<sub>3</sub>) m/z: 471 (M+H)<sup>+</sup>.

**Example 1159B****N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt**

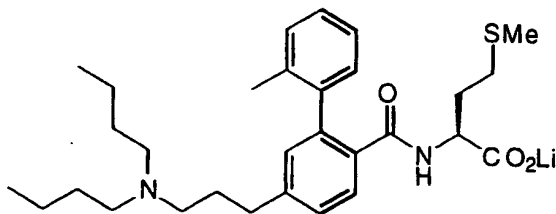
13285 The procedure described in the Example 403I was used here to convert the  
intermediate 1159A (63 mg) to the title lithium salt (62 mg, 100%). <sup>1</sup>H NMR (300 MHz,  
dmso-d<sub>6</sub>) δ 8.10 (t, 1 H), 7.57 (d, 1 H), 7.40 (br d, 1 H), 7.37-7.20 (m, 4 H), 7.17 (br s,  
1 H), 7.04 (br d, 1 H), 3.75 (m, 1 H), 3.54 (s, 2 H), 3.13 (q, 2 H), 2.28-1.85 (m, 8 H),  
1.78 (m, 1 H), 1.64 (m, 1 H), 1.47 (m, 2 H), 1.35 (m, 2 H), 0.93 (t, 3 H). MS(ESI-)  
m/z: 455 (M-H)<sup>-</sup>.

13290

**Example 1160****N-[4-(N-(2,2,4,4-tetramethylbutylamino)carbonylethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt**

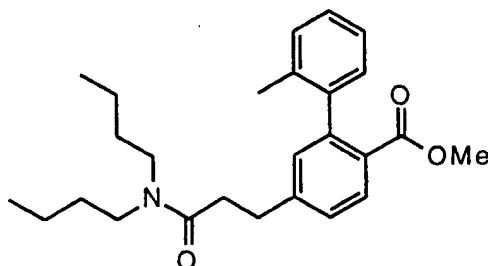
13295

The procedures described in the Example 1147C and 1147D were used here to  
convert 1147B (50 mg) to the title lithium salt (50 mg, 81%, 2 steps). <sup>1</sup>H NMR (300 MHz,  
dmso-d<sub>6</sub>) δ 7.44 (d, 1 H), 7.26 (br s, 1 H), 7.25-7.08 (m, 5 H), 6.98 (br s, 1 H), 6.88 (m,  
1 H), 3.63 (m, 1 H), 2.82 (t, 2 H), 2.32 (t, 2 H), 2.20-1.90 (m, 8 H), 1.75-1.50 (m, 2 H),  
13300 1.67 (s, 2 H), 1.23 (s, 6 H), 0.89 (s, 9 H). MS(ESI-) m/z: 525 (M-H)<sup>-</sup>.



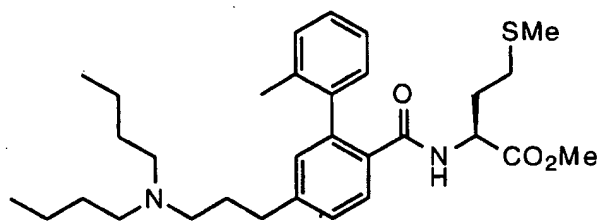
Example 1161

13305

Example 1161AMethyl 4-(N,N-Dibutylaminocarbonyl)ethyl-2-(2-methylphenyl)benzoate

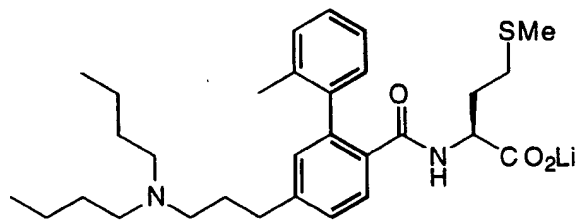
The procedure described in the Example 1144C was used here to convert the intermediate 1144B (150 mg, 0.5 mmol) and dibutylamine (129 mg, 1 mmol) to the title methyl ester (203 mg, 99%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (d, 1 H), 7.29-7.16 (m, 4 H), 7.06 (m, 2 H), 3.60 (s, 3 H), 3.30 (dt, 2 H), 3.14 (t, 2 H), 3.05 (t, 2 H), 2.61 (t, 2 H), 2.05 (s, 3 H), 1.46 (m, 2 H), 1.27 (m, 2 H), 0.90 (t, 6 H). MS(CI/NH<sub>3</sub>) m/z: 410 (M+H)<sup>+</sup>.

13315

Example 1161BN-[4-(N,N-Dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine Methyl Ester

The procedures described in the Example 403E and 403F were used here to convert the above intermediate 1161A (195 mg, 0.48 mmol) to the title methyl ester (165 mg, 66%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.90 (2 d'd, 1 H), 7.35-7.19 (m, 5 H), 7.02 (br s, 1 H), 5.88 (br d, 1 H), 4.61 (m, 1 H), 3.65 (s, 3 H), 2.66 (t, 2 H), 2.40 (m, 6 H), 2.20-2.00 (m, 8 H), 1.90-1.70 (m, 3 H), 1.59 (m, 1 H), 1.45-1.20 (m, 8 H), 0.89 (t, 6 H). MS(CI/NH<sub>3</sub>) m/z: 520 (M+H)<sup>+</sup>.

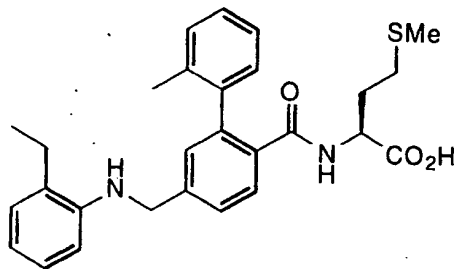
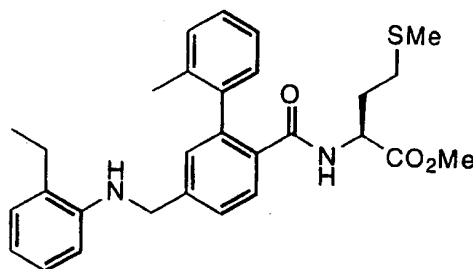
13325



Example 1161CN-[4-(N,N-Dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

13330 The procedure described in the Example 403I was used here to convert the intermediate 1161B (156 mg) to the title lithium salt (151 mg, 98%). <sup>1</sup>H NMR (300 MHz, dmso-d<sub>6</sub>) δ 7.46 (d, 1 H), 7.34-7.08 (m, 5 H), 6.97 (m, 2 H), 3.75 (m, 1 H), 2.63 (t, 2 H), 2.32 (m, 6 H), 2.20-1.80 (m, 9 H), 1.70 (m, 3 H), 1.60 (m, 1 H), 1.38-1.20 (m, 8 H), 0.84 (t, 6 H). MS(ESI-) m/z: 511 (M-H)<sup>-</sup>.

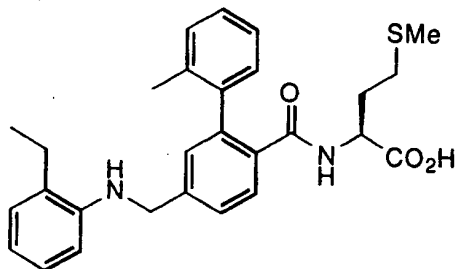
13335

Example 1164

13340

Example 1164AN-[4-N-(2-Ethylphenyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

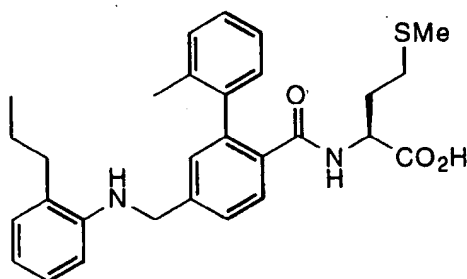
The desired ester was prepared using the method described in Example 403H starting with the compound described in Example 403G and 2-ethylaniline. m/e (ESI) 489 (MH<sup>+</sup>)



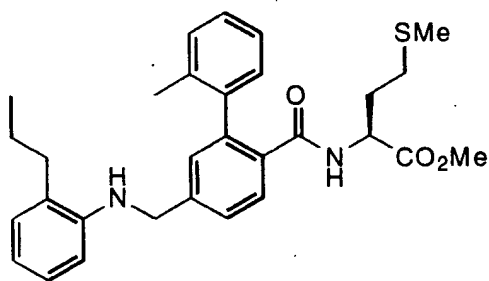
13345

Example 1164BN-[4-N-(2-Ethylphenyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1164A.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.96 (1H, t,  $J=9\text{Hz}$ ), 7.48 (1H, bd,  $J=8\text{Hz}$ ), 7.20-7.00 (8H, m), 6.77 (1H, t,  $J=9\text{Hz}$ ), 6.57 (1H, bd,  $J=8\text{Hz}$ ), 5.89 (1H, bd,  $J=8\text{Hz}$ ), 4.58 (1H, m), 4.46 (2H, s), 2.55 (2H, q,  $J=8\text{Hz}$ ), 2.20-2.00 (8H, m), 1.90 (1H, m), 1.57 (1H, m), 1.25 (3H, t,  $J=8\text{Hz}$ ).  $m/e$  (ESI) 475 ( $\text{MH}^+$ )  
 Anal.calc. for  $\text{C}_{28}\text{H}_{32}\text{N}_2\text{O}_3\text{S}\cdot 0.25\text{H}_2\text{O}$  C 69.90, H 6.81, N 5.82 Found C 69.64, H 6.66, N 5.65



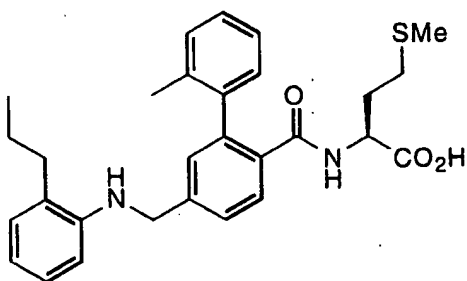
Example 1165



Example 1165A

N-[4-N-(2-Propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

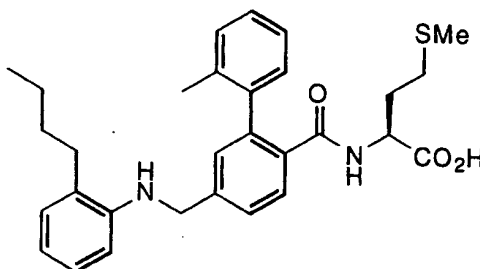
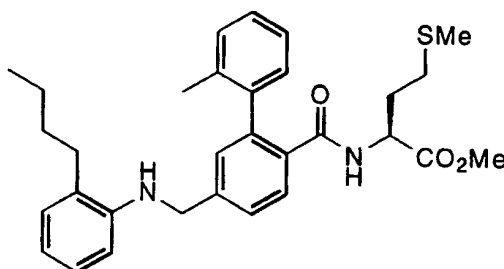
The desired ester was prepared using the method described in Example 403H starting with the compound described in Example 403G and 2-propylaniline.  $m/e$  (ESI) 503 ( $\text{MH}^+$ )



Example 1165B

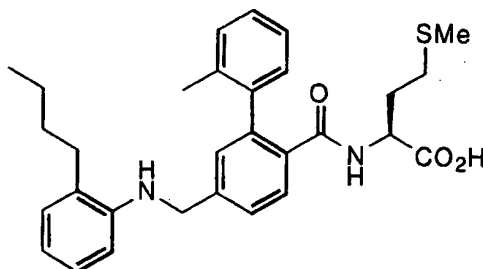
N-[4-N-(2-Propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1165A.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.98 (1H, t,  $J=9\text{Hz}$ ), 7.47 (1H, dd,  $J=8\&2\text{Hz}$ ), 7.40-7.10 (6H, m), 7.03 (2H, m), 6.72 (1H, t,  $J=9\text{Hz}$ ), 6.57 (1H, m), 5.86 (1H, bd,  $J=8\text{Hz}$ ), 4.58 (1H, m), 4.44 (2H, s), 2.48 (2H, t,  $J=8\text{Hz}$ ), 2.20-2.00 (8H, m), 1.91 (1H, m), 1.65 (2H, q,  $J=8\text{Hz}$ ), 1.57 (1H, m), 1.01 (3H, t,  $J=8\text{Hz}$ ).  $m/e$  (ESI) 489 ( $\text{MH}^-$ ) Anal. calc. for  $\text{C}_{29}\text{H}_{34}\text{N}_2\text{O}_3\text{S}\cdot 0.25\text{H}_2\text{O}$  C 70.34, H 7.02, N 5.66 Found C 70.33, H 6.88, N 5.44

Example 1166Example 1166A

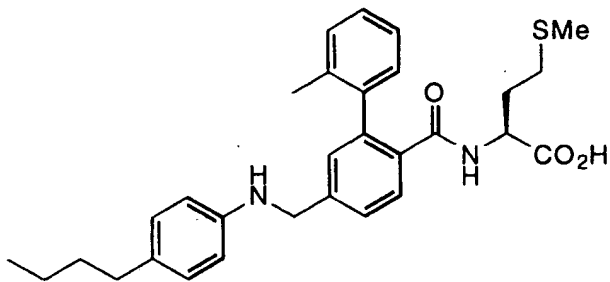
N-[4-N-(2-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired ester was prepared using the method described in Example 403H starting with the compound described in Example 403G and 2-butylaniline.  $m/e$  (ESI) 517 ( $\text{MH}^-$ )

Example 1166B

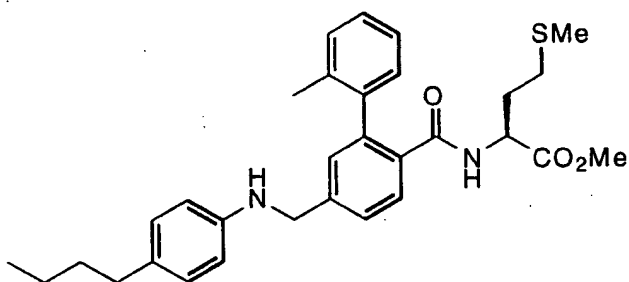
N-[4-N-(2-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

13390 The desired compound was prepared according to the method of Example 403I  
 starting with compound prepared in Example 1166A.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.97 (1H, t,  $J=9\text{Hz}$ ), 7.45 (1H, bd,  $J=8$ ), 7.40-7.10 (6H, m), 6.98 (2H, d,  $J=8\text{Hz}$ ), 6.73 (1H, t,  $J=9\text{Hz}$ ), 6.57 (1H, m), 5.87 (1H, bd,  $J=8\text{Hz}$ ), 4.58 (1H, m), 4.45 (2H, s), 2.50 (2H, t,  $J=8\text{Hz}$ ), 2.20-2.00 (8H, m), 1.91 (1H, m), 1.70-1.50 (3H, m), 1.40 (2H, q,  $J=8\text{Hz}$ ),  
 13395 0.93 (3H, t,  $J=8\text{Hz}$ ). m/e (ESI) 503 ( $\text{MH}^+$ ) Anal. calc. for  $\text{C}_{30}\text{H}_{36}\text{N}_2\text{O}_3\text{S}\cdot 0.50\text{H}_2\text{O}$  C 70.14, H 7.26, N 5.45 Found C 70.39, H 7.08, N 5.24



Example 1167

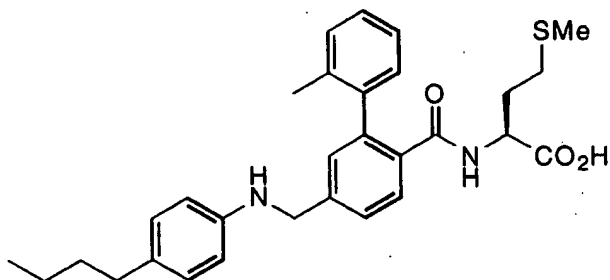
13400



Example 1167A

N-[4-N-(4-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

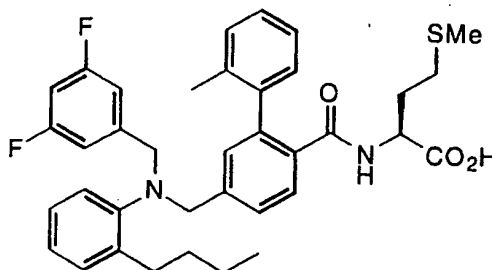
The desired ester was prepared using the method described in Example 403H starting with  
 13405 the compound described in Example 403G and 4-butylaniline. m/e (ESI) 517 ( $\text{MH}^+$ )



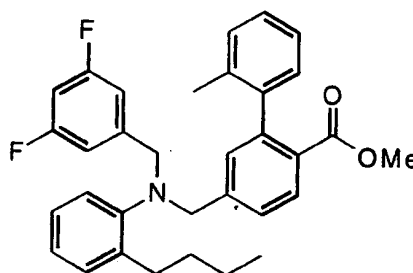
Example 1167B

N-[4-N-(4-Butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

13410 The desired compound was prepared according to the method of Example 403I  
 starting with compound prepared in Example 1167A.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.98 (1H, t,  $J=9\text{Hz}$ ), 7.47 (1H, bd,  $J=8$ ), 7.40-7.10 (6H, m), 7.04 (2H, d,  $J=9\text{Hz}$ ), 6.56 (2H, d,  $J=9\text{Hz}$ ), 5.88 (1H, bd,  $J=8\text{Hz}$ ), 4.57 (1H, m), 4.40 (2H, s), 2.48 (2H, t,  $J=8\text{Hz}$ ), 2.20-  
 13415 2.00 (8H, m), 1.90 (1H, m), 1.53 (3H, m), 1.32 (2H, m), 0.92 (3H, t,  $J=8\text{Hz}$ ).  $m/e$  (ESI) 503 ( $\text{MH}^+$ ) Anal. calc. for  $\text{C}_{30}\text{H}_{36}\text{N}_2\text{O}_3\text{S} \cdot 0.25 \text{H}_2\text{O}$  C 70.76, H 7.23, N 5.50  
 Found C 70.77, H 7.07, N 5.35



13420 Example 1168

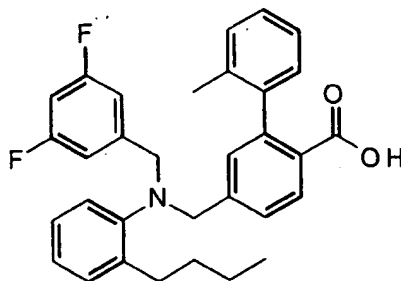


Example 1168A

4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid  
methyl ester

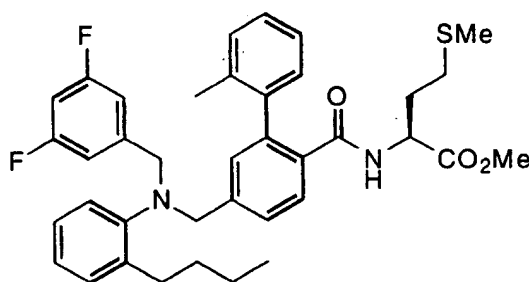
13425 The desired compound was prepared using the method described in Example 1169A  
 starting with 2-butylaniline, 3,5-difluorobenzyl bromide, and 4-bromomethyl-2-(2-  
 methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D.  $m/e$  (ESI) 514  
 13430 ( $\text{MH}^+$ )



Example 1168B

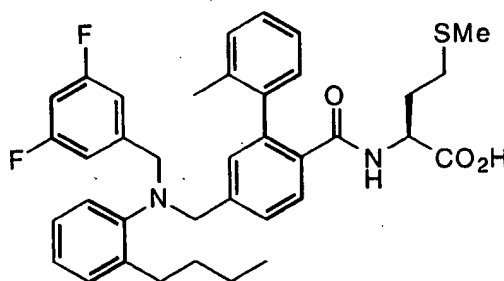
4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid

The desired acid was prepared using the method described in Example 403E starting with the product from Example 1168A.

Example 1168C

N-[4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403F starting with the product from Example 1168B. m/e (ESI) 645 (MH<sup>+</sup>)

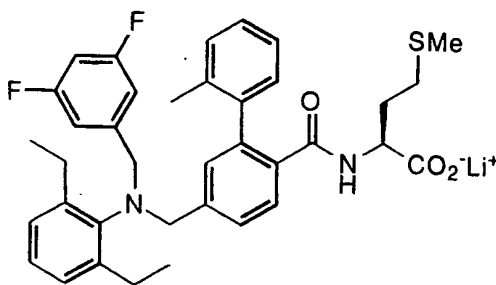
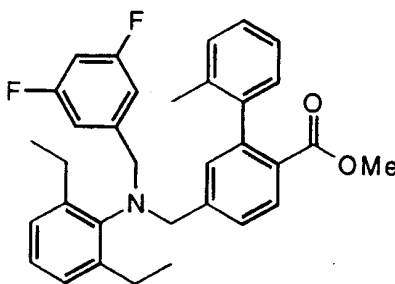
Example 1168D

N-[4-N-(2-Butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1168C. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.92 (1H, m), 7.40-6.90 (10H, m), 6.81 (2H, bd, J=8Hz), 6.66 (1H, m), 5.84 (1H, m), 4.55 (1H, m), 4.12 (2H, s), 4.04 (2H, s), 2.72 (2H, bt, J=9Hz), 2.20-1.80 (9H, m), 1.52 (3H, m), 1.36

(2H, m), 0.87 (3H, t, J=8Hz). m/e (ESI) 629 (MH<sup>+</sup>) Anal.calc. for C<sub>37</sub>H<sub>40</sub>F<sub>2</sub>N<sub>2</sub>O<sub>3</sub>S C 70.45, H 6.39, N 4.40 Found C 70.10, H 6.27, N 4.35

13455

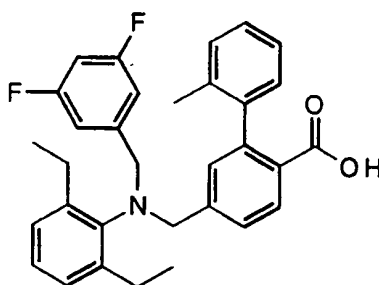
Example 1169Example 1169A

13460

4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

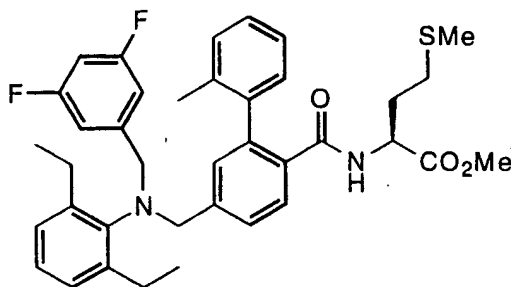
4-Bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester (100 mg, 0.31 mmol), prepared as in Example 1178A-D, 2,6-diethylaniline (0.062 mL, 0.38 mmol), and diisopropylethylamine (0.084 mL, 0.470 mmol) were dissolved in DMF (5 mL), and solution stirred overnight at room temperature. To this mixture was then added diisopropylethylamine (0.084 mL, 0.470 mmol) and  $\alpha$ -bromo-3,5-difluorotoluene (0.100 mL, 0.760 mmol), and reaction heated at 80°C for 3 days. Solvents concentrated in vacuo, and residue purified by flash chromatography on silica gel eluting with 2% EtOAc/Hexanes to afford the desired compound as a yellow oil (72 mg, 45%). m/e (ESI) 514 (MH<sup>+</sup>)

13470

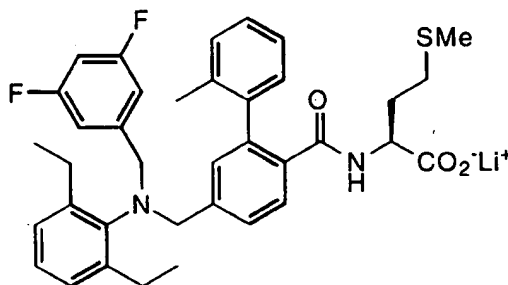


Example 1169B4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoic acid

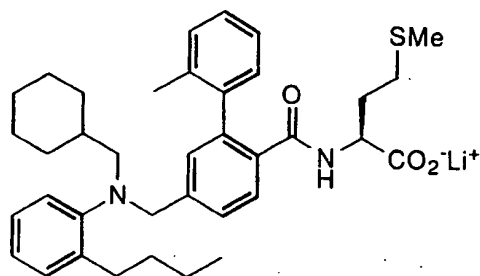
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1169A.

Example 1169CN-[4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

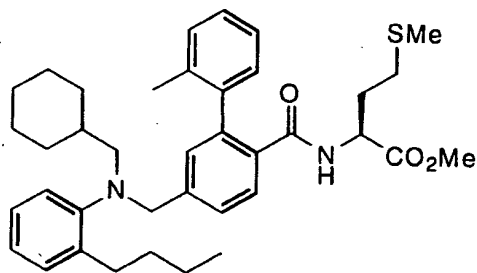
The desired compound was prepared using the method described in Example 403F starting with the product from Example 1169B. m/e (ESI) 645 (MH<sup>+</sup>)

Example 1169DN-[4-N-(2,6-Diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1169C. <sup>1</sup>H (300MHz, DMSO, δ) 7.43 (1H, d, J=9Hz), 7.30-7.00 (9H, m), 6.85 (4H, m), 4.21 (2H, s), 4.18 (2H, s), 3.65 (1H, m), 2.60-2.40 (4H, m), 2.10-1.50 (10H, m), 1.03 (6H, t, J=8Hz). m/e (ESI) 629 (MH<sup>-</sup>)  
 Anal.calc. for C<sub>37</sub>H<sub>39</sub>F<sub>2</sub>LiN<sub>2</sub>O<sub>3</sub>S·1.50 H<sub>2</sub>O C 66.95, H 6.38, N 4.22 Found C 66.79, H 6.34, N 3.93

Example 1170

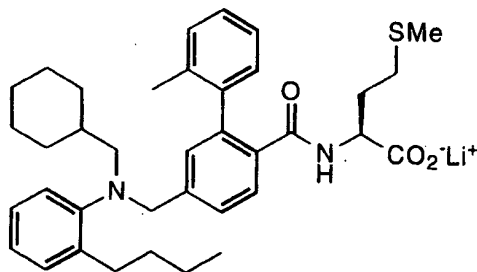
13500

Example 1170A

N-[4-N-(2-Butylphenyl)-N-(cyclohexylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

13505

The desired ester was prepared using the method described in Example 403H starting with the compound described in Example 1166A and cyclohexanecarboxaldehyde. m/e (ESI) 613 (MH<sup>-</sup>)

Example 1170B

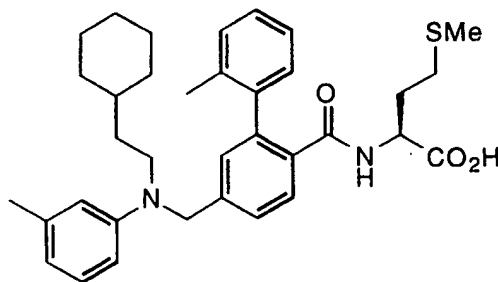
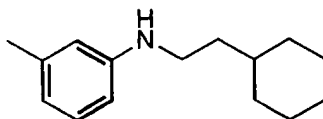
13510

N-[4-N-(2-Butylphenyl)-N-(cyclohexylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1170A. <sup>1</sup>H (300MHz, DMSO, δ) 7.47 (1H, d, J=9Hz), 7.29 (1H, m), 7.25-6.95 (9H, m), 6.90 (1H, m), 3.97 (2H, s), 3.16 (1H, m), 2.70 (4H, m), 2.10-1.85 (7H, m), 1.70 (3H, m), 1.60-1.40 (6H, m), 1.40-1.15 (4H, m), 1.05 (3H, m), 0.79 (5H, t, J=8Hz). m/e (ESI) 599 (MH<sup>-</sup>) Anal.calc. for C<sub>37</sub>H<sub>47</sub>LiN<sub>2</sub>O<sub>3</sub>S·1.00 H<sub>2</sub>O C 71.13, H 7.90, N 4.48 Found C 71.01, H 7.93, N 4.14

13515

13520

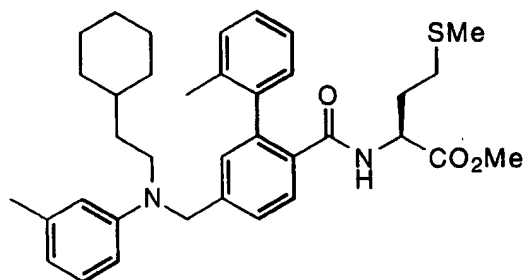
Example 1171Example 1171AN-(2-Cyclohexylethyl)-N-(3-methylphenyl)amine

13525

13530

13535

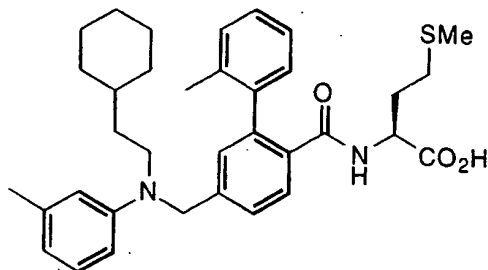
To a stirred solution at ambient temperature of cyclohexylacetic acid (500 mg, 3.52 mmol) and 3-methylaniline (0.45 mL, 4.22 mmol) in DMF (10 mL) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (809 mg, 4.22 mmol). Reaction stirred overnight at ambient temperature. Reaction diluted with EtOAc and washed with water, 1.0M NaHCO<sub>3</sub> (2x), 1N H<sub>3</sub>PO<sub>4</sub> (2x), and brine. Organic layer dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. To a solution at ambient temperature under N<sub>2</sub> of this residue in anhydrous THF (3 mL) was added a 1.0M lithium aluminum hydride solution (7.00 mL, 7 mmol) in THF. Reaction refluxed overnight. Reaction cooled to 0°C and quenched with successive addition of water (0.27 mL), 15% aqueous NaOH (0.27 mL), and water (0.80 mL). Mixture stirred 30 minutes at ambient temperature, and solids filtered off through celite and washed with EtOAc. Filtrate dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo to produce a colorless oil. m/e (DCI/NH<sub>3</sub>) 218 (MH<sup>+</sup>)

Example 1171B

13540

N-[4-N-(2-Cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

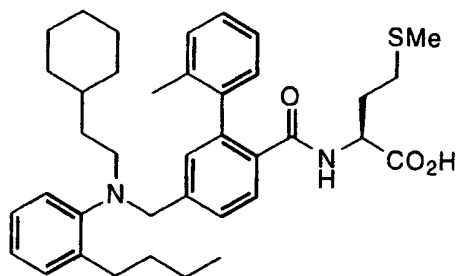
The desired ester was prepared using the method described in Example 403H starting with the compounds described in Example 403G and Example 1171A. m/e (ESI) 585 (MH<sup>+</sup>)



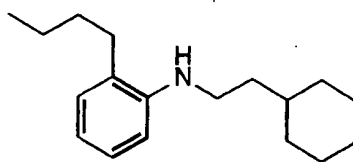
Example 1171C

N-[4-N-(2-Cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1171B. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.92 (1H, t, J=9Hz), 7.40-7.00 (8H, m), 6.47 (2H, m), 5.86 (1H, d, J=8Hz), 4.51 (4H, m), 3.39 (2H, m), 2.25 (3H, s), 2.15-1.80 (8H, m), 1.70 (5H, m), 1.50 (3H, m), 1.40-1.05 (4H, m), 0.96 (2H, m). m/e (ESI) 571 (MH<sup>+</sup>) Anal. calc. for C<sub>35</sub>H<sub>44</sub>N<sub>2</sub>O<sub>3</sub>S·1.00 H<sub>2</sub>O C 71.15, H 7.85, N 4.74 Found C 70.91, H 7.89, N 4.46



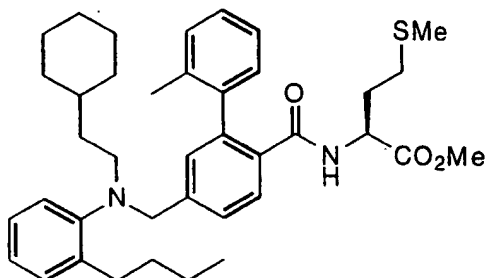
Example 1172



Example 1172A

N-(2-Butylphenyl)-N-(2-cyclohexylethyl)amine

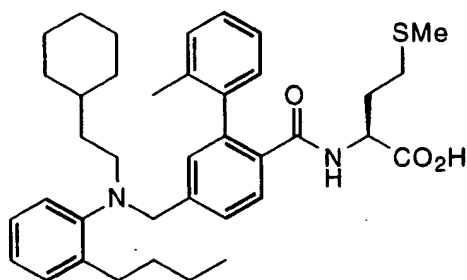
13565 The desired amine was prepared using the method described in Example 1171A starting with cyclohexylacetic acid and 2-butylaniline. m/e (DCI/NH<sub>3</sub>) 260 (MH<sup>+</sup>)



Example 1172B

13570 N-[4-N-(2-Butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

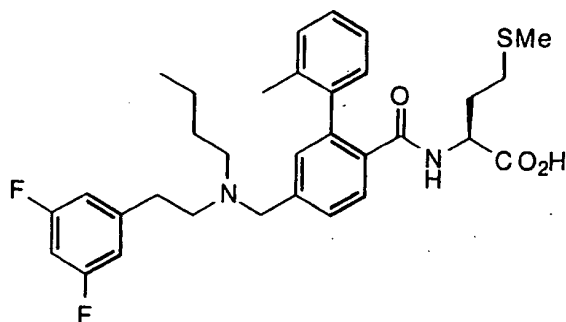
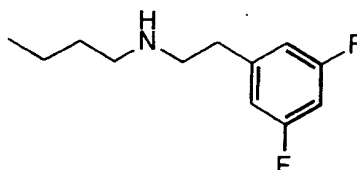
The desired ester was prepared using the method described in Example 403H starting with the compounds described in Example 403G and Example 1172A. m/e (ESI) 627 (MH<sup>-</sup>)



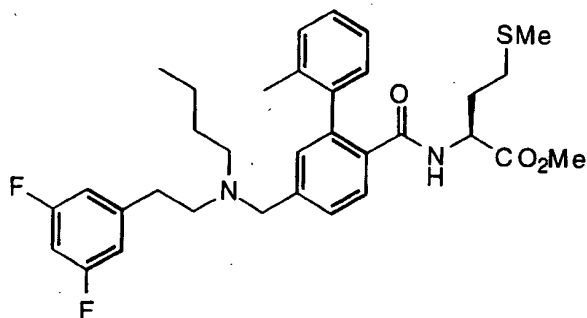
Example 1172C

N-[4-N-(2-Butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1172B. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.94 (1H, t, J=9Hz), 7.41 (1H, bd, J=8HZ), 7.40-7.00 (9H, m), 5.85 (1H, dd, J=8&2Hz), 4.55 (1H, m), 4.07 (2H, s), 2.91 (2H, m), 2.68 (2H, m), 2.20-1.80 (9H, m), 1.70-1.40 (8H, m), 1.40-1.00 (8H, m), 0.86 (3H, t, J=8Hz), 0.79 (2H, m). m/e (ESI) 613 (MH<sup>-</sup>) Anal.calc. for C<sub>38</sub>H<sub>50</sub>N<sub>2</sub>O<sub>3</sub>S·0.25 H<sub>2</sub>O C 73.69, H 8.22, N 4.52 Found C 73.74, H 8.17, N 4.30

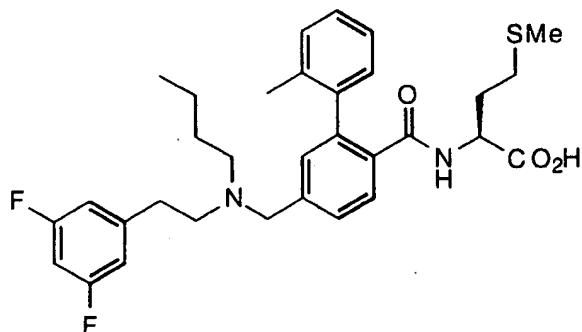
Example 1173Example 1173AN-(2-Butylphenyl)-N-(2-(3,5-difluorophenylethyl)amine

The desired amine was prepared using the method described in Example 1171A starting with 3,5-difluorophenylacetic acid and butylamine. m/e (DCI/NH<sub>3</sub>) 214 (MH<sup>+</sup>)

Example 1173BN-[4-N-Butyl-N-(2-(3,5-difluorophenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-L-methionine methyl ester

The desired ester was prepared using the method described in Example 403H starting with the compounds described in Example 403G and Example 1173A. m/e (ESI) 581 (MH<sup>-</sup>)



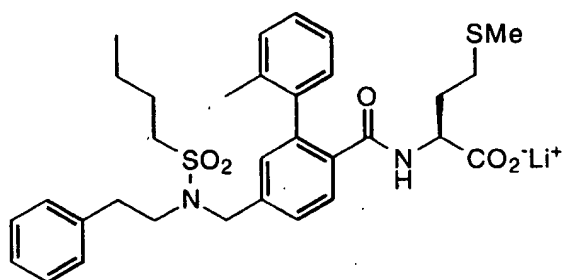
Example 1173C

13605

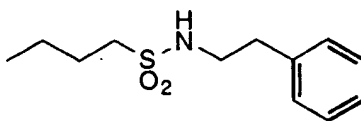
N-[4-N-Butyl-N-(2-(3,5-difluorophenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1173B.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.80 (1H, d,  $J=9\text{Hz}$ ), 7.54 (1H, m), 7.40-7.00 (5H, m), 6.80-6.60 (3H, m), 6.17 (1H, m), 4.43 (1H, m), 4.00 (2H, m), 2.98 (4H, m), 2.81 (2H, m), 2.20-1.80 (9H, m), 2.60 (3H, m), 1.30 (2H, m), 0.92 (3H, t,  $J=8\text{Hz}$ ).  $m/e$  (ESI) 567 ( $\text{MH}^+$ ) Anal. calc. for  $\text{C}_{32}\text{H}_{38}\text{F}_2\text{N}_2\text{O}_3\text{S} \cdot 0.50 \text{H}_2\text{O}$  C 66.53, H 6.80, N 4.85 Found C 66.67, H 6.67, N 4.69

13610



13615

Example 1174Example 1174A

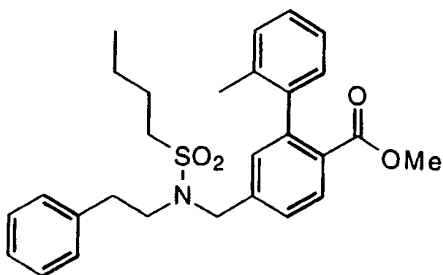
13620

N-(Butanesulfonyl)-N-(2-phenylethyl)amine

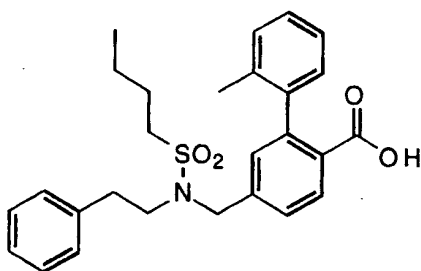
To a stirred solution at ambient temperature of phenethylamine (200 mg, 1.65 mmol) in  $\text{CH}_2\text{Cl}_2$  (2 mL) was added triethylamine (0.35 mL, 2.48 mmol) and butanesulfonyl chloride (0.24 mL, 1.82 mmol). After 4 hours of stirring at ambient temperature, the reaction was diluted with EtOAc and washed with water, 1.0M  $\text{NaHCO}_3$ , and brine.

13625

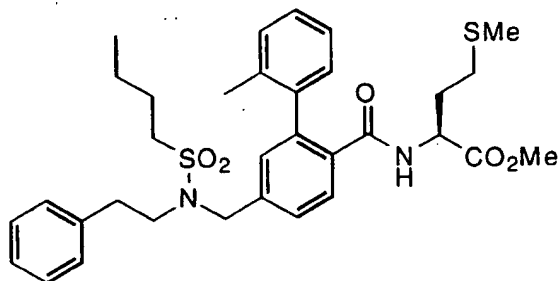
Organic layer dried with  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo.

Example 1174B4-(N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

To a stirred mixture in anhydrous DMF (1 mL) at room temperature under N<sub>2</sub> of 60% sodium hydride suspension in mineral oil (30 mg, 0.752) was added N-(butanesulfonyl)-N-(2-phenylethyl)amine (181 mg, 0.752 mmol), prepared as in Example 1174A. Reaction stirred 20 minutes, and then, a solution of 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester (200 mg, 0.627 mmol), prepared as in Example 1178A-D, in anhydrous DMF (5 mL) was added. Reaction stirred overnight at room temperature. Reaction quenched with 1N H<sub>3</sub>PO<sub>4</sub> and diluted with EtOAc. Organic layer separated, washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel (15% EtOAc/Hexanes) to afford the desired product as a pale yellow oil (293 mg, 98%). m/e (ESI) 480 (MH<sup>+</sup>)

Example 1174C4-(N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

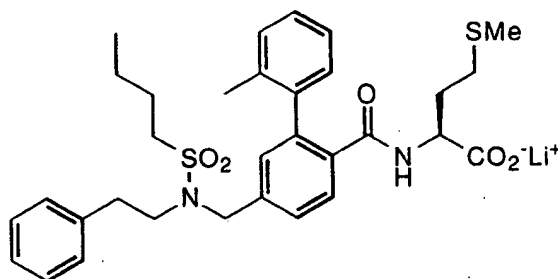
The desired acid was prepared using the method described in Example 403E starting with the product from Example 1174B.

Example 1174D

13650

N-[4-N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403F starting with the product from Example 1174C. m/e (ESI) 480 (MH<sup>+</sup>)

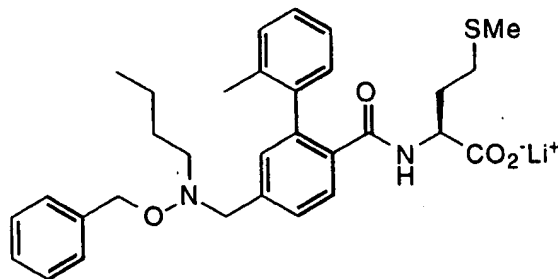


13655

Example 1174E

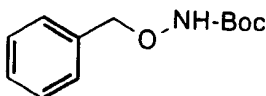
N-[4-N-Butanesulfonyl-N-(2-phenylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1174D. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.62 (1H, d, J=7Hz), 7.52 (1H, dd, J=7&2Hz), 7.20-7.10 (10H, m), 7.14 (1H, bd, J=7Hz), 4.65 (2H, bs), 3.76 (1H, m), 3.00 (2H, m), 2.78 (2H, m), 2.25-2.00 (5H, m), 1.99 (3H, s), 1.90-1.70 (4H, m), 1.62 (2H, m), 1.37 (2H, m), 0.92 (3H, t, J=8Hz). m/e (ESI) 595 (MH<sup>+</sup>) Anal.calc. for C<sub>32</sub>H<sub>39</sub>LiN<sub>2</sub>O<sub>5</sub>S<sub>2</sub>·0.50 H<sub>2</sub>O C 62.83, H 6.59, N 4.38 Found C 62.59, H 6.59, N 4.44



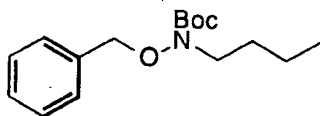
Example 1175

13670 *N*-[4-*N*--Benzyloxy-*N*-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1175A

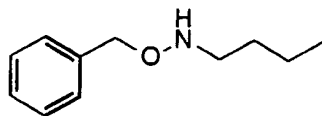
13675 *N*--t-Butoxycarbonyl-*O*-benzylhydroxylamine

To a stirred solution at 0°C of *O*-benzylhydroxylamine hydrochloride in THF was added diisopropylethylamine (2.5 equiv.) and di-*t*-butyldicarbonate (1.2 equiv.). Reaction stirred one hour at 0°C and overnight at ambient temperature. Reaction concentrated *in vacuo*. Residue taken up in EtOAc and washed with water, 1.0M NaHCO<sub>3</sub>, 1N H<sub>3</sub>PO<sub>4</sub>, and brine. Organic layer dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated.

Example 1175B

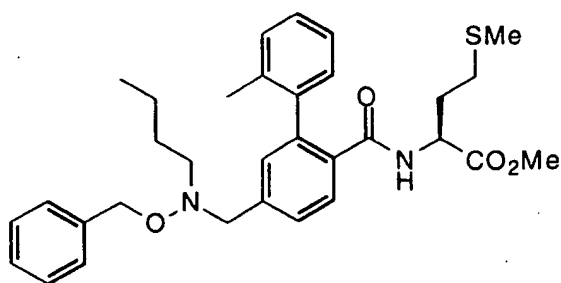
*N*--t-Butoxycarbonyl-*N*-butyl-*O*-benzylhydroxylamine

13685 To a stirred solution at 0°C of *N*--t-Butoxycarbonyl-*O*-benzylhydroxylamine, prepared as in Example 1175A, in anhydrous THF was added portionwise a 60% dispersion of sodium hydride (1.2 equiv.) in mineral oil. Mixture stirred 30 minutes at 0°C, and then, 1-iodobutane (1.2 equiv.) was added dropwise. Reaction stirred one hour at 0°C, and then, overnight at room temperature. Reaction concentrated *in vacuo*. Residue taken up in EtOAc and washed with water, 1.0M NaHCO<sub>3</sub>, 1N H<sub>3</sub>PO<sub>4</sub>, and brine. Organic layer dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated.

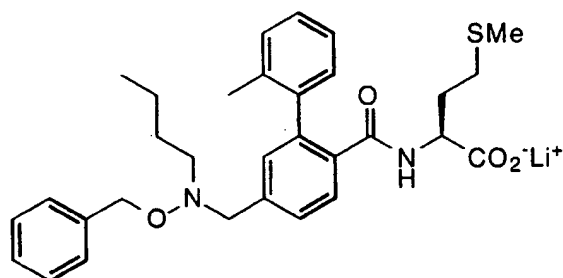
Example 1175C

13695 *N*-Butyl-*O*-benzylhydroxylamine hydrochloride salt

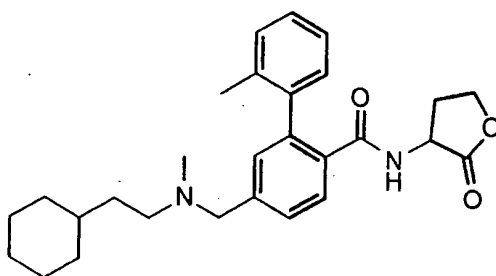
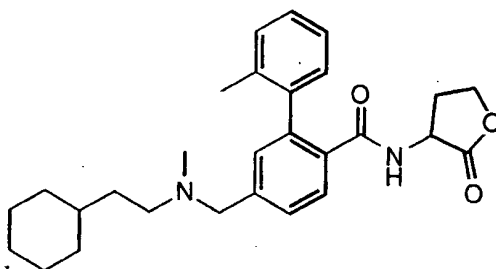
The desired compound was prepared using the method described in Example 403D starting with the compound prepared in Example 1175B.

Example 1175DN-[4-N--Benzyloxy-N-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired ester was prepared using the method described in Example 403H starting with the compound prepared in Example 1175C and N-[4-Formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI) 547 (MH<sup>-</sup>)

Example 1175EN-[4-N--Benzyloxy-N-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

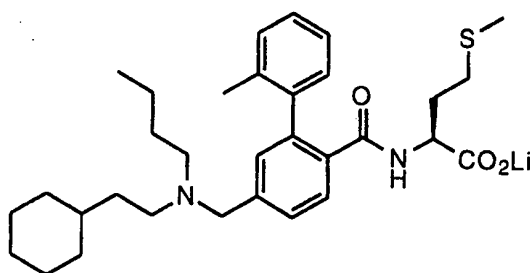
The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1175D. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.52 (1H, d, J=9Hz), 7.40 (1H, dd, J=7&2Hz), 7.30-7.10 (10H, m), 6.96 (1H, bd, J=7Hz), 4.46 (2H, bs), 3.87 (2H, bs), 3.71 (1H, m), 2.68 (2H, t, J=8Hz), 2.25-1.95 (5H, m), 1.93 (3H, s), 1.90-1.60 (2H, m), 1.50 (2H, m), 1.30 (2H, m), 0.83 (3H, t, J=8Hz). m/e (ESI) 533 (MH<sup>-</sup>) Anal.calc. for C<sub>31</sub>H<sub>37</sub>LiN<sub>2</sub>O<sub>4</sub>S·0.75 H<sub>2</sub>O C 67.19, H 7.00, N 5.05 Found C 67.19, H 6.91, N 4.96

Example 1177Example 1177

N-[4-N-(2-Cyclohexylethyl)-N-methylaminomethyl]-2-(2-methylphenyl)benzoyl]-3-aminotetrahydrofuran-2-one

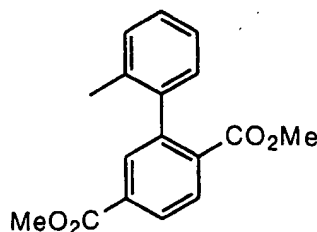
The desired compound was prepared using the method of Example 403F starting with 4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoic acid, prepared as in Example 608C, and  $\alpha$ -amino- $\gamma$ -butyrolactone hydrobromide.

$^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) (rotamer) 7.91 (1H, t,  $J=9\text{Hz}$ ), 7.41 (1H, bd,  $J=8\text{Hz}$ ), 7.35-7.20 (4H, m), 7.19 (1H, d,  $J=2\text{Hz}$ ), 5.72 (1H, m), 4.49 (1H, m), 4.33 (1H, bt,  $J=8\text{Hz}$ ), 4.17 (1H, m), 3.53 (2H, s), 2.62 (1H, m), 2.39 (2H, t,  $J=8\text{Hz}$ ), 2.20 (3H, s), 2.15 (2.07) (3H, s), 1.80-1.50 (7H, m), 1.38 (2H, m), 1.30-1.10 (3H, m), 0.89 (2H, m).  $m/e$  (ESI) 447 ( $\text{MH}^+$ ) Anal. calc. for  $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}_3 \cdot 1.00 \text{ H}_2\text{O}$  C 72.07, H 8.21, N 6.00 Found C 72.12, H 8.03, N 5.76

Example 1178

N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

Lithium Salt



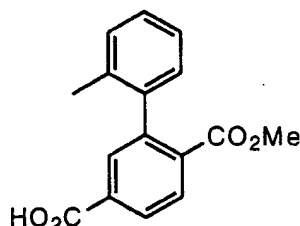
13745

Example 1178A

Dimethyl-(2-methylphenyl)terephthalate

A mixture of dimethyliodoterephthalate (278 g, 0.87 mol), 2-methylphenylboronic acid (141 g, 1.04 mol) palladium (II) acetate (1.95 g, 0.0087 mol) and triphenylphosphine (9.1 g, 0.035 mol) in 2.2 L of toluene and 2.2 L of 2M sodium carbonate was degassed with nitrogen and heated to 80°C for 1.5 hours and cooled to ambient temperature. The layers were separated and the organic layer filtered through a plug of silica gel (600g) prewetted with methyl t-butylether (MTBE, 1.2 L). The frit was washed with 5 L of MTBE. The mixture was then concentrated to provide 237 g (96%) of the title compound. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.09, dd, 1H; 8.02, d, 1H; 7.95, d, 1H; 7.20 - 7.34, m, 3H; 7.10, bd, 1H; 3.96, s, 3H; 3.64, s, 3H; 2.08, s, 3H. MS (DCI/NH<sub>3</sub>) 302 (M + NH<sub>4</sub>)<sup>+</sup>.

13755



Example 1178B

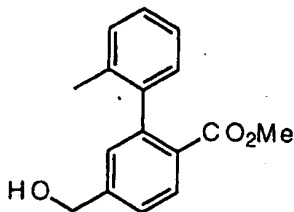
2-(2-methylphenyl)-4-carboxybenzoic acid, methyl ester

13760

A solution of example 1178A (194 g, 0.68 mol) in 2:1 THF/methanol (~0.3M) was cooled to 0°C and lithium hydroxide (0.38 L of a 2.2 M aqueous solution, 0.82 mol) was added such that the reaction temperature remained below 10°C. The cooling bath was removed and the mixture allowed to warm to 11°C overnight and then warmed to ~20°C over 4 hours. The mixture was concentrated to a volume of ~1.2 L and then diluted to 5.6 L with water. The mixture was extracted with hexanes and the aqueous layer filtered through celite (~200 g) and the celite pad washed with water. The mixture was diluted with ethyl acetate (6 L) and the pH of the aqueous phase adjusted to 5.5 by the addition of 3M aqueous HCl (~250 mL). The organic phase was removed and concentrated to provide 171 g (93%) of the

13765

- 13770 title compound. The material was ~ 87% pure. An analytical sample was obtained by recrystallization from aqueous ethanol.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.14, dd, 1H; 8.03, d, 1H; 8.01, d, 1H; 7.28 - 7.42, m, 3H; 7.09, bd, 1H; 3.64, s, 3H; 2.08, s, 3H. MS ( $\text{DCI}/\text{NH}_3$ ): 271 ( $\text{MH}$ ) $^+$ ; 288 ( $\text{M} + \text{NH}_4$ ) $^+$ .



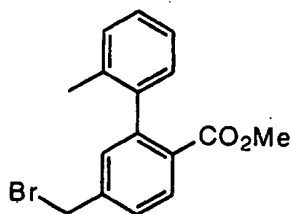
13775

#### Example 1178C

##### 4-hydroxymethyl-2-(2-methylphenyl)benzoic, methyl ester

- 13780 A solution of example 1178B (4.67g, 17.3 mmol) in 35 mL of THF was cooled in an ice bath and treated with borane (0.88M in THF, 39 mL, 34.6 mmol) such that the internal temperature remained below 10°C. The cooling bath was removed and the solution stirred for 3 hours and then cooled in an ice bath. The reaction was quenched by the careful addition of 8 mL of water (vigorous evolution of hydrogen gas) keeping the temperature below 10°C. An additional 8 mL of water was added and the mixture partitioned between ethyl acetate and 2N sodium hydroxide. The layers were separated and the organic layer was
- 13785 extracted with water, dried, filtered and concentrated. The residue was purified by column chromatography on silica gel to provide 3.90 g (88%) of the title compound.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.98, d, 1H; 7.43, dd, 1H; 7.16 - 7.28, m, 4H; 7.07, bd, 1H; 4.77, s, 2H; 3.62, s, 3H; 2.05, s, 3H; 1.78, bs, 1H. MS ( $\text{DCI}/\text{NH}_3$ ): 257 ( $\text{MH}$ ) $^+$ ; 274 ( $\text{M} + \text{NH}_4$ ) $^+$ .

13790



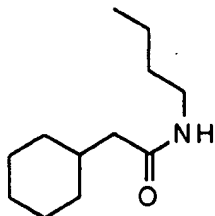
#### Example 1178D

##### 4-bromomethyl-2-(2-methylphenyl)benzoic, methyl ester

- 13795 A solution of 36 g (140 mmol) of example 1178C and 13.4 g (154 mmol) lithium bromide in DMF (150 mL) was chilled in an ice-water bath, then 40.3 g (14.0 mL, 149 mmol) phosphorous tribromide was added, followed by more DMF (50 mL). After 15 minutes the reaction was partitioned between water (1200 mL) and  $\text{Et}_2\text{O}$  (600 mL). The aqueous layer was extracted with  $\text{Et}_2\text{O}$  (2 x 150 mL), then the combined  $\text{Et}_2\text{O}$  layers were



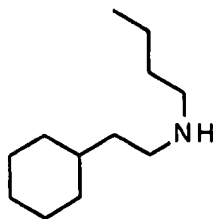
washed with brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration, recovered 44.5 g (97.5%) slightly cloudy, almost colorless oil that was 2% DMF by weight (determined by NMR). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.84 (d, 1H), 7.44 (dd, 1H), 7.24 (m, 4H), 7.07 (br d, 1H), 4.50 (s, 2H), 3.62 (s, 3H), 2.07 (s, 3H). MS (DCI/NH<sub>3</sub>) 336/338 (M+H+NH<sub>3</sub>)<sup>+</sup>.



Example 1178E

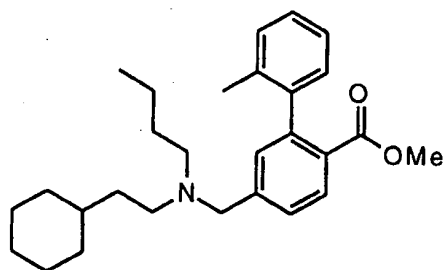
N-butyl-N-2-cyclohexylacetamide

2-Cyclohexylacetic acid (42.66 g, 0.30 mol) was dissolved in 85 mL of thionyl chloride and the mixture heated to reflux for 2 hours. After cooling to room temperature, the yellow solution was concentrated. Toluene was added and the solution was concentrated again and the acid chloride used directly. The acid chloride was diluted with 100 mL of methylene chloride and this solution added to a biphasic mixture of butylamine (60 mL, 0.60 mol) in 100 mL of methylene chloride and 2M aqueous potassium carbonate (150 mL) and the mixture was stirred overnight at ambient temperature. An additional 30 mL of butylamine was added and stirring continued for 2 hours and then the mixture was poured into a separatory funnel. The layers were separated and the aqueous phase was extracted with 1 portion of methylene chloride and the combined organic extracts were dried, filtered and concentrated to an off white solid. This material was suspended in 400 mL of 1:1 ether/hexanes and filtered. The solid was washed with 2 additional portions of 1:1 ether/hexanes. The filtrates were extracted with 3 portions of aqueous HCl, dried, filtered and concentrated to a volume of ~ 200 mL. The solid that formed was collected by filtration and combined with the previous solid material and dried under vacuum to give the title compound (49.50 g, 88%). <sup>1</sup>H nmr (300 MHz., CDCl<sub>3</sub>): δ 5.35, bs, 1H; 3.24, q, 2H; 2.02, d, 2H; 1.70, bm, 6H; 1.47, m, 2H; envelope 1.06 - 1.42, 5H; 0.91, m, 5H. MS (DCI-NH<sub>3</sub>): 198 (MH<sup>+</sup>); 215 (M+NH<sub>4</sub><sup>+</sup>).



Example 1178FN-butyl-N-2-cyclohexylethylamine

13830 A stirred suspension of lithium aluminum hydride (23.74 g, 0.63 mol) in THF (400 mL) was cooled in an ice bath and treated with a solution of example 1178E (49.50 g, 0.26 mol) in THF (300 mL). The ice bath was removed and the mixture heated to gentle reflux for 20 hours. The solution was cooled in an ice bath and quenched by the careful addition of 24 mL of water in 100 mL of THF, followed by 24 mL of 15% aqueous sodium hydroxide, 13835 followed by an additional 72 mL of water. The thick slurry was vigorously stirred for 15 minutes at which time 600 mL of methylene chloride and excess sodium sulfate were sequentially added. The mixture was stirred for 1 hour and then filtered through celite. The celite pad was washed well with methylene chloride and the filtrate concentrated to give the title compound (47.80 g, 100%) which was sufficiently pure for the next step. <sup>1</sup>H nmr (300 13840 MHz., CDCl<sub>3</sub>): δ 2.61, m, 4H; 1.69, m, 5H; envelope 1.05 - 1.53, 11H; 0.91, m, 5H. MS (DCI-NH<sub>3</sub>): 184 (MH<sup>+</sup>).

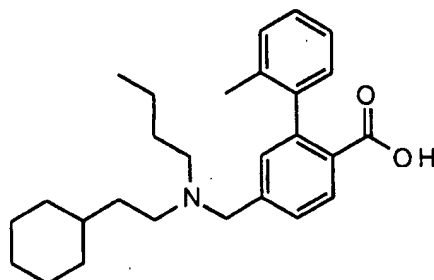
Example 1178G

13845 4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoic acid, methyl ester

A solution of example 1178D (22.2 g, 0.070 mol) and diisopropylethylamine (15.7 mL, 0.090 mol) in 100 mL of acetonitrile was treated with N-butyl-N-2-cyclohexylethylamine (15.3 g, 0.084 mol). The cloudy mixture was stirred for two hours and then briefly warmed to ~45°C. After cooling to ambient temperature, the mixture was 13850 concentrated to remove the acetonitrile and then diluted with 400 mL of water. The pH of the mixture was brought to >10 with solid potassium phosphate and extracted with 3 portions of ethyl ether. The combined ether extracts were extracted with 1 portion of water and two 13855 portions of brine, dried, filtered and concentrated. The residue obtained (34.4 g, 117%) was used directly. An analytical sample was obtained by column chromatography on silica gel (3% ethyl acetate/hexanes) to provide pure material. <sup>1</sup>H nmr (300 MHz., CDCl<sub>3</sub>): δ 7.92, d, 1H; 7.48, dd, 1H; 7.16 - 7.28, m, 4H; 7.07, bd, 1H; 3.62, s, 3H; 3.57, s, 2H; 2.41,

quartet, 4H; 2.06, s, 3H; 1.62, bm, 5H; envelope 1.05 - 1.48, 10H; 0.85, bm, 5H. MS (ESI+): 422 (MH<sup>+</sup>); (ESI-): 420 (M-H).

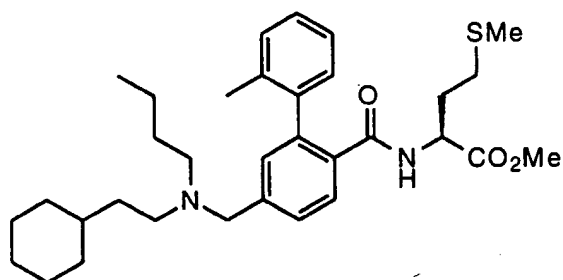
13860



#### Example 1178H

##### N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)]benzoic acid

13865 A solution of 1178G (34.35 g, 0.081 mol) in 210 mL of ethanol was treated with aqueous sodium hydroxide (4N, 70 mL, 0.28 mol) and the mixture heated to reflux until judged complete by tlc analysis. After cooling to room temperature, the mixture was concentrated to remove the ethanol. The resulting solid was partially dissolved by adding water and the mixture extracted with ethyl ether. The ether layer was then washed with water and then with 1M aqueous phosphoric acid which resulted in an oily precipitate. The  
13870 precipitate was dissolved by extracting with 3 portions of ethyl acetate and the combined ethyl acetate layer were washed with water, 0.5M aqueous phosphoric acid, brine and then dried, filtered and concentrated to give 24.5 g, (86% yield for the two steps) as a cream colored solid. <sup>1</sup>H nmr (300 MHz., CD<sub>3</sub>OD): δ 7.96, d, 1H; 7.64, dd, 1H; 7.37, d, 1H; 7.22, m, 2H; 7.18, m, 1H; 7.07, d, 1H; 4.41, bs, 2H; 3.12, m, 4H; 2.10, s, 3H; 1.18, bm, 9H; 1.37, sextet, 2H; 1.23, m, 3H; 0.96, t, 3H; 0.94, m, 2H. MS (ESI+): 408 (MH<sup>+</sup>);  
13875 (ESI-): 406 (M-H).

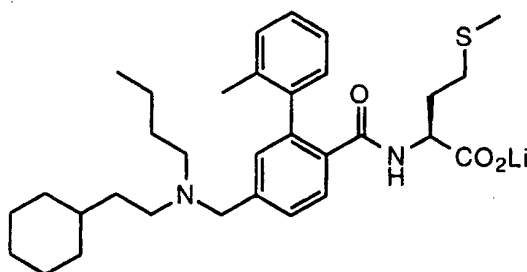


#### Example 1178I

##### N-[4-(N-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

13880 Partitioned 13.2 g (66.1 mmol) L-methionine methyl ester, hydrochloride salt between saturated aqueous NaHCO<sub>3</sub> (80 mL) and CH<sub>2</sub>Cl<sub>2</sub> (75 mL). Added the organic

layer to the following solution: 24.5 g (60.2 mmol) acid from Example 1178H, 10.0 g (65.3 mmol) HOBT•H<sub>2</sub>O, and 12.6 g (65.7 mmol) EDCI•HCl in DMF (150 mL). After stirring at RT overnight partitioned the reaction between saturated aqueous NaHCO<sub>3</sub> (500 mL) and EtOAc (1200 mL). The organic layer was washed with water and brine, then dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration, recovered 30 g orange oil that was purified by chromatography using hex/EtOAc 3/1. Recovered 22.9 g (69%) of the title compound. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.90 (m, 1H), 7.40 (d, 1H), 7.30, 7.20, 7.16 (all m, total 5H), 5.88 (br d, 1H), 4.62 (m, 1H), 3.66 (s, 3H), 3.57 (s, 2H), 2.41 (m, 4H), 2.18, 2.13, 2.04 (s, m, m, total 9H), 1.85 (m, 1H), 1.62 (m, 5H), 1.50-1.10 (envelope, 10H), 0.87 (m, 5H). MS (APCI) 553 (M+H)<sup>+</sup>.



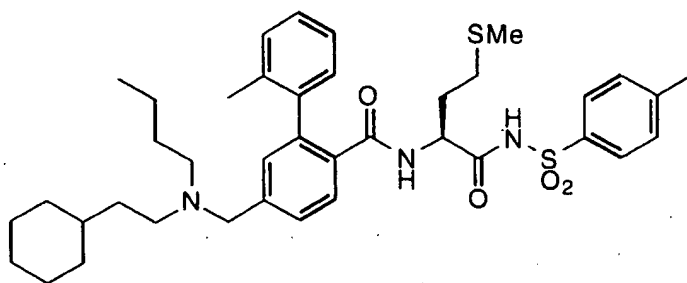
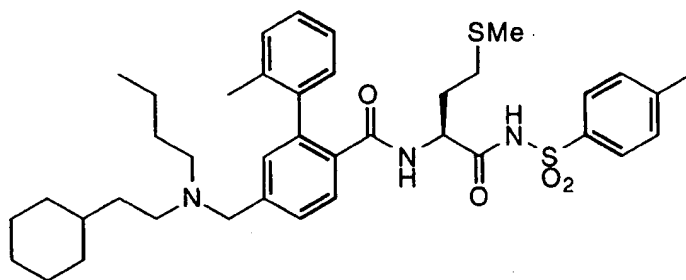
#### Example 1178J

N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine.

#### Lithium Salt

A solution of example 1178I (22.9 g, 0.041 mol), in 200 mL of 3:1 THF methanol was cooled in an ice bath and then treated with aqueous lithium hydroxide (1M, 83 mL, 0.083 mol) dropwise. The ice bath was removed and the mixture was stirred for 20 hours. The solution was concentrated to remove the organics and the resulting thick slurry diluted with water until a clear solution resulted (~1.2 L). The pH of the solution was carefully adjusted to pH~5 with 1M aqueous phosphoric acid and stirred for 1 hour. The solid was collected by filtration and dried under vacuum over phosphorous pentoxide to provide 19.93 g of a cream colored solid. This material was dissolved in 200 mL of THF and treated with a solution of 1.55 g (0.037 mol) of lithium hydroxide in 75 mL of water. The mixture was stirred for 15 minutes and the THF removed under vacuum on a rotary evaporator. The mixture was diluted with 500 mL of water and lyophilized to give 20.10 g (89% overall) of the title compound. <sup>1</sup>H nmr (300 MHz., CD<sub>3</sub>OD): δ 7.64, m, 1H; 7.41, d, 1H; 7.05 - 7.32, m, 5H; 4.25, m, 1H; 3.69, s, 2H; 2.52, m, 4H; 2.51, s, 1.5H (1/2 o-tolyl); 2.06, s, 1.5 H (1/2 o-tolyl); 1.98, s, 3H; 1.97, m, 1H; 1.73, m, 2H; 1.64, bm, 6H; envelope 1.04 - 1.56, 10H; 0.90, m, 5H. MS (ESI<sup>+</sup>): 539 (MH<sup>+</sup>); (ESI<sup>-</sup>): 537 (M-H). Calc'd for C<sub>32</sub>H<sub>45</sub>N<sub>2</sub>O<sub>3</sub>SLi•0.60 H<sub>2</sub>O; C 69.19; H 8.38; N 5.04; Found: C 69.25; H 8.50; N 4.99.

13915

Example 1179

13920

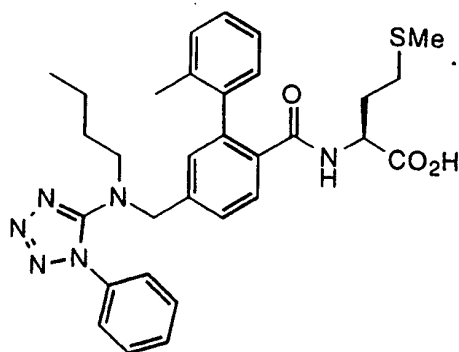
Example 1179

N-[4-(N-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine  
4-methylphenylsulfonimide

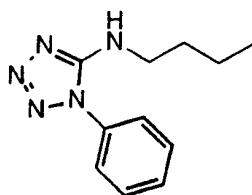
13925 N-[4-(N-Butyl-N-(2-Cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine (500 mg, 0.929 mmol), prepared as in Example 1178, p-toluenesulfonamide (429 mg, 2.51 mmol), 4-dimethylaminopyridine (57 mg, 0.465 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (214 mg, 1.12 mmol) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at room temperature and stirred overnight. Reaction diluted with water and CHCl<sub>3</sub> and layers separated. Aqueous layer extracted with CHCl<sub>3</sub> (2x), and combined

13930 extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 300:1 EtOAc/25:1:1 EtOAc, H<sub>2</sub>O, AcOH to afford the desired compound as a white solid (284 mg, 44%). <sup>1</sup>H (300MHz, MeOD, δ) (rotamer) 7.73 (2H, d, J=9Hz), 7.62 (1H, d, J=8Hz), 7.48 (1H, bd, J=8Hz), 7.30-7.00 (7H, m), 4.22 (1H, m), 4.02 (2H, bs), 2.81 (4H, m), 2.39 (3H, s), 2.21(2.03) (3H, bs),

13935 1.90 (3H, s), 1.85-1.40 (13H, m), 1.40-1.10 (6H, m), 0.93 (5H, t, J=8Hz). m/e (ESI) 690 (MH<sup>+</sup>) Anal.calc. for C<sub>39</sub>H<sub>53</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>·1.25 H<sub>2</sub>O C 65.56, H 7.83, N 5.88 Found C 65.41, H 7.52, N 5.61



13940

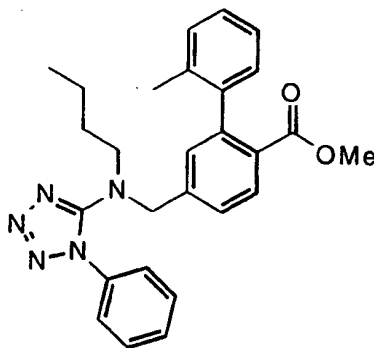
Example 1180Example 1180A

13945

N-Butyl-N-(1-phenyltetrazol-5-yl)amine

5-Chloro-1-phenyl-1H-tetrazole (1.00 g, 5.54 mmol), butylamine (0.547 mL, 5.54 mmol), and diisopropylethylamine (1.48 mL, 8.31 mmol) were dissolved in DMF (5 mL), and stirred overnight at room temperature. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 35% EtOAc/Hexanes to afford the desired product as a white solid (625 mg, 52%). m/e (DCI) 218 (MH<sup>+</sup>)

13950

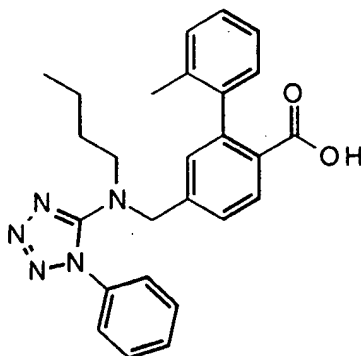
Example 1180B

13955

4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

The desired compound was prepared according to the method of Example 1174B starting with 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D, and the compound from Example 1180A.

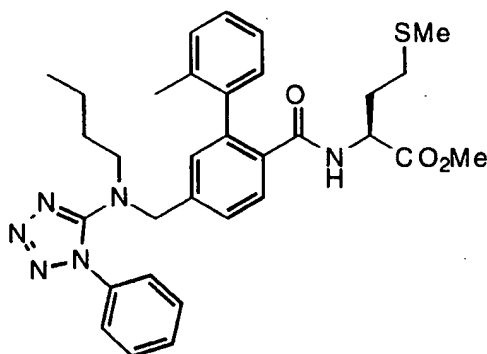
13960

Example 1180C

4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoic acid

The desired acid was prepared using the method described in Example 403E starting with the product from Example 1180B. m/e (ESI) 440 (MH<sup>-</sup>)

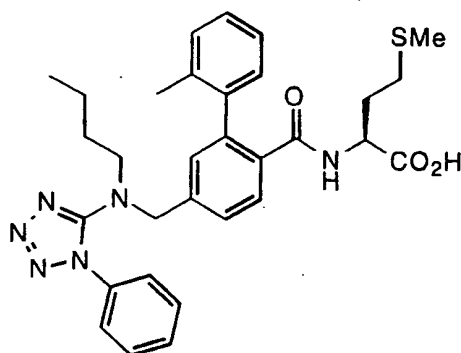
13965

Example 1180D

N-[4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

13970

The desired compound was prepared using the method described in Example 403F starting with the product from Example 1180C. m/e (ESI) 587 (MH<sup>+</sup>)

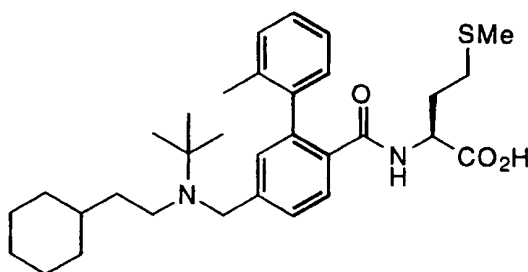
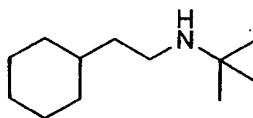


13975

Example 1180EN-[4-N-Butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1180D. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.93 (1H, m), 7.60-7.40 (5H, m), 7.40-7.10 (5H, m), 7.03 (1H, d, J=2Hz), 5.89 (1H, m), 4.55 (1H, m), 4.52 (2H, s), 3.11 (2H, bt, J=8Hz), 2.20-2.00 (8H, m), 1.90 (1H, m), 1.56 (1H, m), 1.43 (2H, m), 1.06 (2H, m), 0.74 (3H, t, J=8Hz). m/e (ESI) 571 (MH<sup>+</sup>) Anal.calc. for C<sub>31</sub>H<sub>36</sub>N<sub>6</sub>O<sub>3</sub>S C 65.01, H 6.34, N 14.67 Found C 64.77, H 6.33, N 14.70

13985

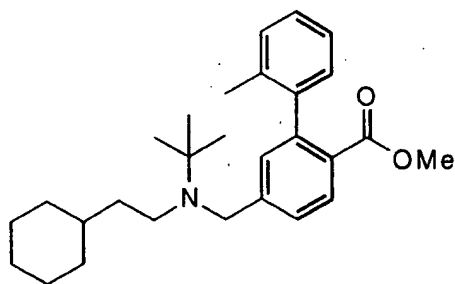
Example 1181

13990

Example 1181AN-t-Butyl-N-(2-cyclohexylethyl)amine

The desired amine was prepared using the method described in Example 1171A starting with cyclohexylacetic acid and t-butylamine. m/e (DCI/NH<sub>3</sub>) 184 (MH<sup>+</sup>)



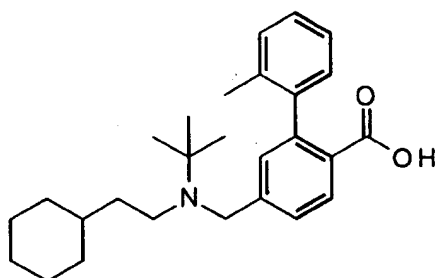


13995

Example 1181B

4-(N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

14000 The desired compound was prepared using the method described in Example 1178G starting with N-t-butyl-N-(2-cyclohexylethyl)amine, prepared as in Example 1181A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D. m/e (ESI) 422 (MH<sup>+</sup>)

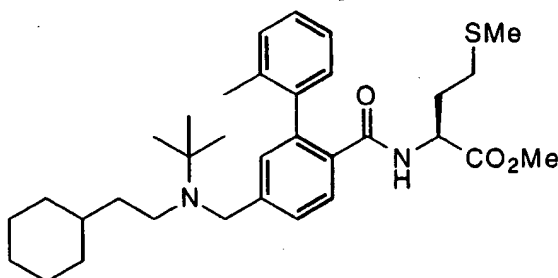


14005

Example 1181C

4-(N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

The desired acid was prepared using the method described in Example 403E starting with the compound prepared in Example 1181B.

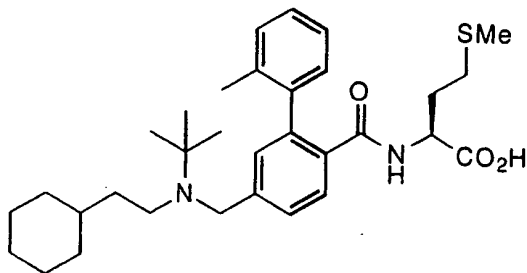


14010

Example 1181D

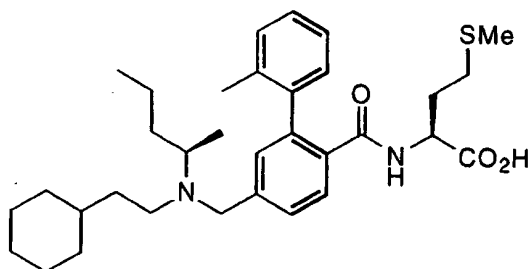
N-[4-N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

14015 The desired product was prepared using the method described in Example 403F starting with the compound prepared in Example 1181C. m/e (ESI) 553 (MH<sup>+</sup>)

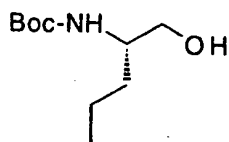
Example 1181E

N-[4-N-t-Butyl-N-(2-cyclohexylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

14020 The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1181D.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.78 (1H, m), 7.67 (1H, m), 7.40-7.00 (5H, m), 6.21 (1H, m), 4.38 (1H, m), 4.13 (2H, m), 2.93 (2H, m), 2.20-2.00 (7H, m), 2.00 (3H, s), 1.60 (4H, m), 1.43 (12H, bs), 1.40-0.90 (4H, m), 0.75 (2H, m).  $m/e$  (ESI) 537 ( $\text{MH}^+$ ) Anal. calc. for  $\text{C}_{32}\text{H}_{46}\text{N}_2\text{O}_3\text{S} \cdot 0.75 \text{H}_2\text{O}$  C 69.59, H 8.67, N 5.07 Found C 69.78, H 8.65, N 4.89

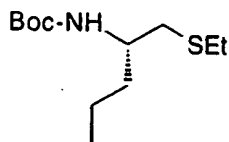
Example 1182

14030

Example 1182A

(2S)-t-Butoxycarbonylaminopentan-1-ol

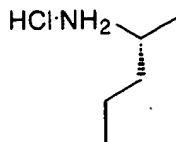
14035 The desired product was prepared using the methods described in Example 1183A starting with L-norvaline.



Example 1182B(2S)-t-Butoxycarbonylamino-1-ethylthiopentane

14040

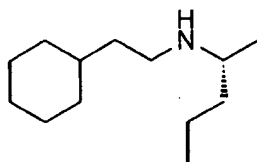
The desired product was prepared using the methods described in Example 403B and 403C starting with the compound prepared in Example 1182A.

Example 1182C

14045

(2R)-Aminopentane hydrochloride salt

The desired product was prepared using the methods described in Example 1183C starting with the compound prepared in Example 1182B.

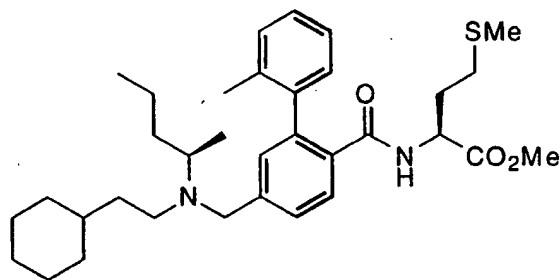
Example 1182D

14050

N-(2-Cyclohexylethyl)-N-(pent-2-yl)amine

The desired amine was prepared using the method described in Example 1171A, except triethylamine was added, starting with cyclohexylacetic acid and the compound from Example 1182C. m/e (DCI) 198 (MH<sup>+</sup>)

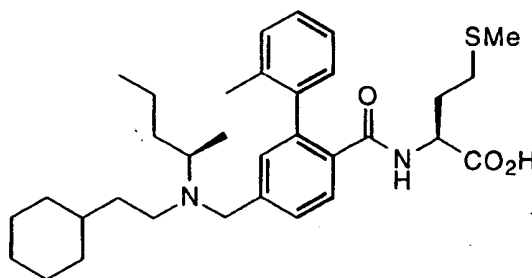
14055

Example 1182E

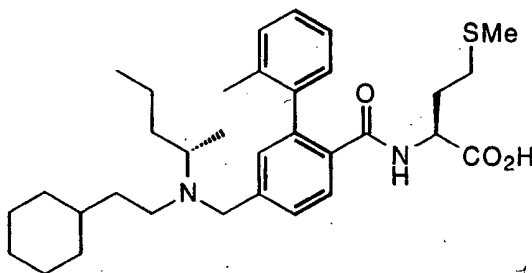
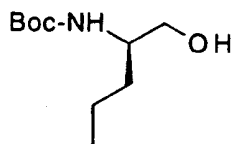
N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

14060

The desired product was prepared using the method described in Example 403H starting with the compound prepared in Example 1182D and N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI) 567 (MH<sup>+</sup>)

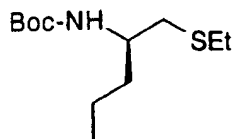
**Example 1182F****N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine**

The desired compound was prepared according to the method of Example 403I starting with the compound prepared in Example 1182E. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.74 (1H, m), 7.62 (1H, m), 7.40-7.00 (5H, m), 6.46 (1H, m), 4.37 (1H, m), 3.94 (2H, m), 3.37 (1H, m), 2.90 (2H, m), 2.20-1.80 (8H, m), 1.80-1.60 (6H, m), 1.55-1.25 (6H, m), 1.25-1.00 (8H, m), 0.91 (3H, t, J=8Hz), 0.82 (2H, m). m/e (ESI) 551 (MH<sup>+</sup>) Anal. calc. for C<sub>33</sub>H<sub>48</sub>N<sub>2</sub>O<sub>3</sub>S·0.50 H<sub>2</sub>O C 70.55, H 8.79, N 4.99 Found C 70.55, H 8.71, N 4.87

**Example 1183****Example 1183A****(2R)-t-Butoxycarbonylaminopentan-1-ol**

To a stirred solution at ambient temperature of D-norvaline (5.00 g, 42.7 mmol) in THF (100 mL) was added an aqueous 4N NaOH solution (21 mL, 84 mmol), di-t-butyl dicarbonate (11.2 g, 51.2 mmol), and tetrabutylammonium bromide (1.0 g). Two-phase solution stirred overnight at ambient temperature. Reaction neutralized with aqueous 3N HCl to pH 6 and extracted with CHCl<sub>3</sub> (3x). Extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo to produce a colorless oil. To a stirred solution at 0°C under N<sub>2</sub> of the

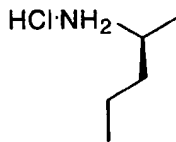
14090 crude residue in anhydrous THF (80 mL) was added dropwise via addition funnel a 1.0M  
borane-THF complex (100 mL, 100 mmol) in THF. After stirring overnight at ambient  
temperature, reaction cooled back to 0°C and quenched with an aqueous 4N NaOH solution  
(50 mL). Mixture stirred one hour at ambient temperature, and then, extracted with CH<sub>2</sub>Cl<sub>2</sub>  
(3x). Extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Residue purified by  
14095 flash chromatography on silica gel eluting with 30% EtOAc/Hexanes to afford the alcohol as  
a pale yellow oil (3.87 g, 45%). m/e (DCI) 204 (MH<sup>+</sup>)



Example 1183B

(2R)-t-Butoxycarbonylamino-1-ethylthiopentane

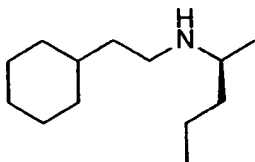
14100 The desired product was prepared using the methods described in Example 403B and  
403C starting with the compound prepared in Example 1183A. m/e (DCI) 248 (MH<sup>+</sup>)



Example 1183C

(2S)-Aminopentane hydrochloride salt

14105 To a stirred solution at ambient temperature of (2R)-t-butoxycarbonylamino-1-  
ethylthiopentane (655 mg, 2.65 mmol), prepared as in Example 1183B, in EtOH (5 mL)  
was added a 50% slurry of Raney Nickel (2.65 g) in water. Mixture stirred vigorously at  
80°C for 2 days. Reaction filtered through celite, and celite and catalyst washed with EtOAc.  
14110 Filtrate concentrated in vacuo to produce a colorless liquid. Residue taken up in a solution of  
4N HCl in dioxane (5 mL), and reaction stirred overnight at ambient temperature. Ether  
added until a solid precipitated. Solid filtered off, washed with ether, and dried to produce  
the desired compound as a white solid (167 mg, 59%).

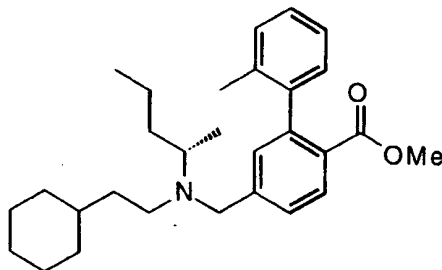


14115

Example 1183D

N-(2-Cyclohexylethyl)-N-(pent-2-yl)amine

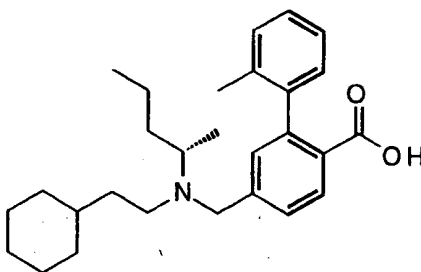
The desired amine was prepared using the method described in Example 1171A, except triethylamine was added, starting with cyclohexylacetic acid and the compound  
 14120 from Example 1183C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  2.70-2.50 (m, 4H), 1.80-1.60 (m, 6H), 1.50-1.00 (m, 8H), 1.04 (d, 3H,  $J=8\text{Hz}$ ), 1.00-0.80 (m, 5H)



#### Example 1183E

14125 N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl]-2-(2-methylphenyl)benzoic acid methyl ester

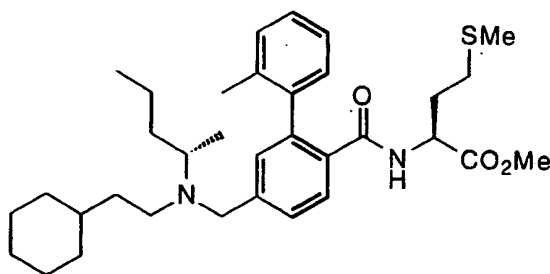
The desired compound was prepared using the method described in Example 1178G starting with N-(2-cyclohexylethyl)-N-(1-methylbutyl)amine, prepared as in Example 1183D, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as  
 14130 in Example 1178A-D. m/e (ESI) 436 ( $\text{MH}^+$ )



#### Example 1183F

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl]-2-(2-methylphenyl)benzoic acid

14135 The desired acid was prepared using the method described in Example 403E starting with the compound prepared in Example 1183E.

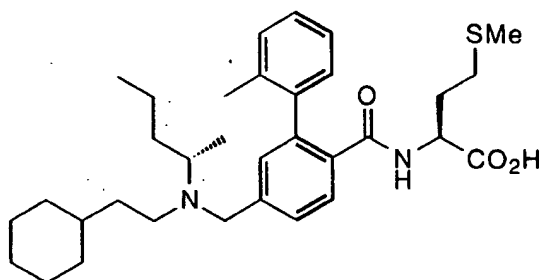


Example 1183G

14140

N-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired product was prepared using the method described in Example 403F starting with the compound prepared in Example 1183F. m/e (ESI) 567 (MH<sup>+</sup>)

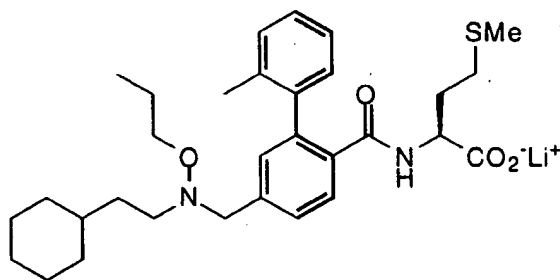
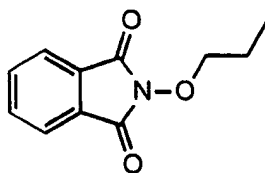


14145

Example 1183HN-[4-N-(2-Cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1183G. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.69 (2H, m), 7.40-7.00 (5H, m), 6.46 (1H, m), 4.38 (1H, m), 4.05 (2H, m), 3.41 (1H, m), 2.90 (2H, m), 2.20-1.75 (9H, m), 1.75-1.50 (7H, m), 1.50-1.00 (12H, m), 0.90 (5H, m). m/e (ESI) 551 (MH<sup>+</sup>) Anal.calc. for C<sub>33</sub>H<sub>48</sub>N<sub>2</sub>O<sub>3</sub>S·0.50 H<sub>2</sub>O C 70.55, H 8.79, N 4.99 Found C 70.65, H 8.63, N 4.93

14155

Example 1184

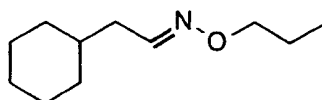
14160

Example 1184A

N-Propoxyphthalimide

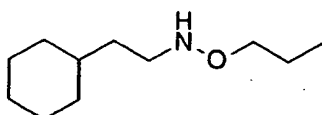
The desired product was prepared using the method described in Example 1176A starting with N-hydroxyphthalimide and 1-propanol. m/e (DCI) 223 (MH+NH<sub>3</sub><sup>+</sup>)

14165

Example 1184BO-Propyl-2-cyclohexylacetaldoxime

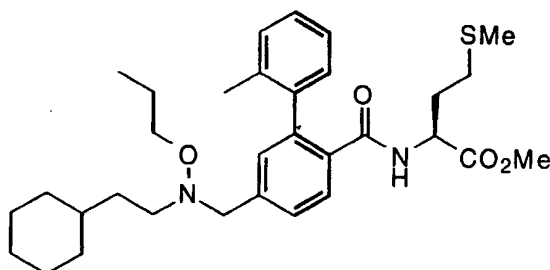
The desired product was prepared using the method described in Example 1176B starting with the compound from Example 1184 A and cyclohexylacetaldehyde.

14170

Example 1184CN--(2-Cyclohexylethyl)-N-propyloxyamine

The desired product was prepared using the method described in Example 1176C starting with the compound from Example 1184B. m/e (DCI) 186 (MH<sup>+</sup>)

14175

Example 1184D

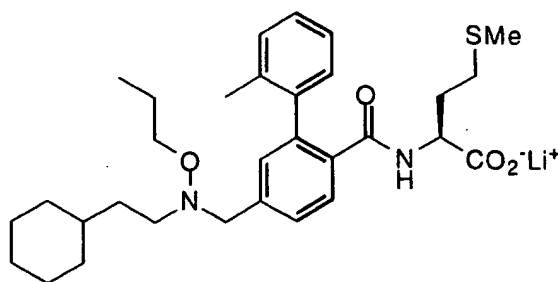
N-[4-N--(2-Cyclohexylethyl)-N-propyloxyaminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired product was prepared using the method described in Example 403H starting with the compound from Example 1184C and N-[4-Formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI)

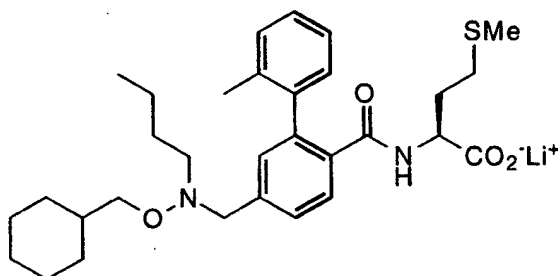
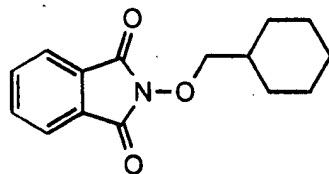
14185

553 (MH<sup>-</sup>)

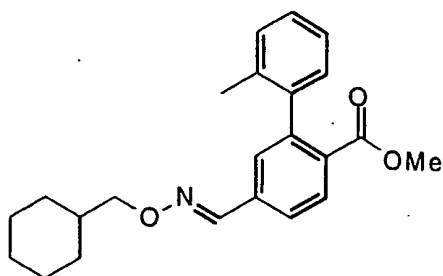


Example 1184EN-[4-N--(2-Cyclohexylethyl)-N-propyloxymethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1184D. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.53 (1H, d, J=9Hz); 7.38 (1H, dd, J=7&2Hz), 7.30-7.00 (5H, m), 6.92 (1H, m), 3.82 (2H, bs), 3.71 (1H, m), 3.41 (2H, m), 2.67 (2H, bt, J=8Hz), 2.25-1.95 (5H, m), 1.91 (3H, s), 1.90-1.50 (7H, m), 1.37 (5H, m), 1.15 (3H, m), 0.86 (2H, m), 0.76 (3H, t, J=8Hz). m/e (ESI) 539 (MH<sup>+</sup>) Anal. calc: for C<sub>31</sub>H<sub>43</sub>LiN<sub>2</sub>O<sub>4</sub>S·0.50 H<sub>2</sub>O C 67.00, H 7.98, N 5.04 Found C 66.82, H 7.75, N 4.92.

Example 1185Example 1185AN-Cyclohexylmethoxyphthalimide

The desired product was prepared using the method described in Example 1176A starting with N-hydroxyphthalimide and cyclohexylmethanol.



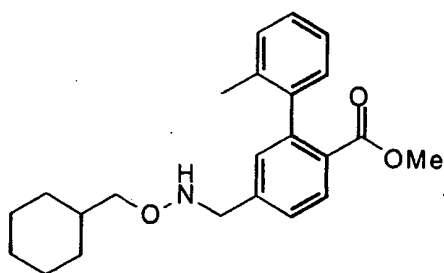
14210

Example 1185B

N-(Cyclohexylmethoxy)aminomethylidene-2-(2-methylphenyl)benzoic acid methyl ester

The desired product was prepared using the method described in Example 1176B starting with the compound from Example 1185A and N-[4-Formyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared using the method of Example 403G and starting with the alcohol prepared in Example 1178C.

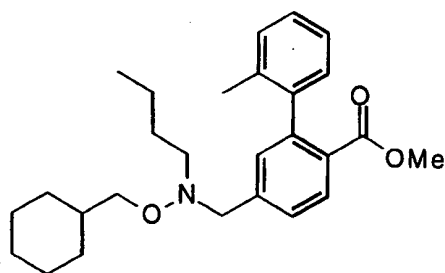
14215

Example 1185C

N-(Cyclohexylmethoxy)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

14220

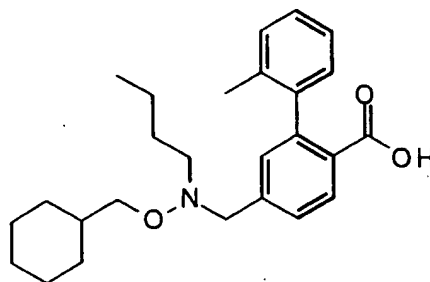
The desired product was prepared using the method described in Example 1176C starting with the compound in Example 1185B. m/e (ESI) 368 (MH<sup>+</sup>)

Example 1185D

N-[4-N--Butyl-N-(cyclohexylmethoxy)aminomethyl]-2-(2-methylphenyl)benzoic acid methyl ester

14225

The desired product was prepared using the method described in Example 1176D starting with the compound in Example 1185C. m/e (ESI) 424 (MH<sup>+</sup>)



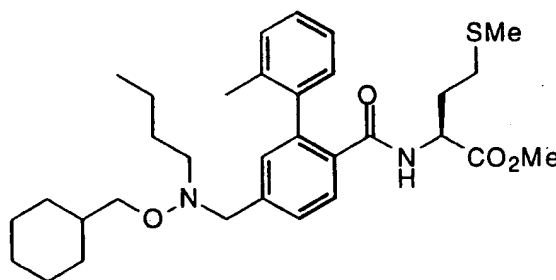
14230

Example 1185E

N-[4-N--Butyl-N-(cyclohexylmethoxy)aminomethyl-2-(2-methylphenyl)benzoic acid

The desired product was prepared using the method described in Example 403E, starting with the compound in Example 1185D.

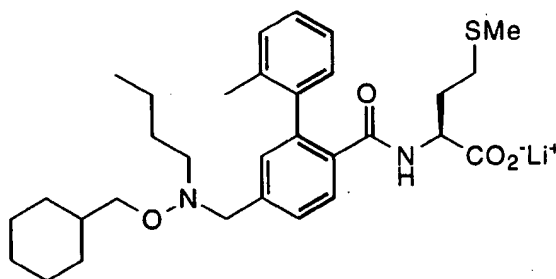
14235

Example 1185F

N-[4-N--Butyl-N-(cyclohexylmethoxy)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

14240

The desired product was prepared using the method described in Example 403F starting with the compound in Example 1185E. m/e (ESI) 555 (MH<sup>+</sup>)

Example 1185G

N-[4-N--Butyl-N-(cyclohexylmethoxy)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

14245

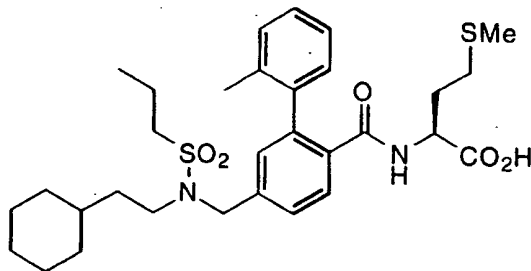
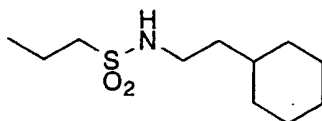
The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1185F. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.51 (1H, d, J=9Hz), 7.37 (1H, bd), 7.30-7.05 (5H, m), 6.94 (1H, m), 3.82 (2H, bs), 3.68 (1H, m),

14250

3.25 (2H, m), 2.64 (2H, t, J=8Hz), 2.25-1.95 (5H, m), 1.93 (3H, s), 1.90-1.40 (9H, m),

1.31 (3H, m), 1.06 (3H, m), 0.85 (3H, t, J=8Hz), 0.73 (2H, m). m/e (ESI) 539 (MH<sup>+</sup>)  
 Anal.calc. for C<sub>31</sub>H<sub>43</sub>LiN<sub>2</sub>O<sub>4</sub>S·2.00 H<sub>2</sub>O C 63.90, H 8.13, N 4.81 Found C 63.63, H 7.68, N 4.62

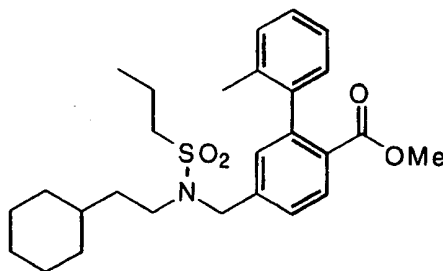
14255

Example 1187

14260

Example 1187AN-(2-Cyclohexylethyl)-N-propanesulfonylamine

The desired product was prepared using the method described in Example 1174A starting with cyclohexylethylamine and 1-propanesulfonyl chloride.

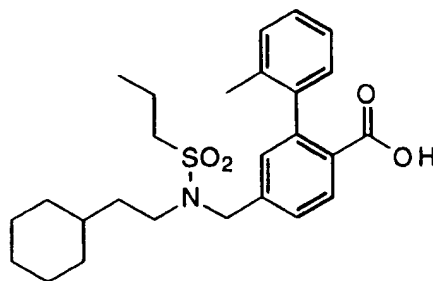


14265

Example 1187B4-(N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

The desired product was prepared using the method described in Example 1174B starting with N-(2-cyclohexylethyl)-N-propanesulfonylamine, prepared as in Example 1187A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D. m/e (ESI) 472 (MH<sup>+</sup>)

14270

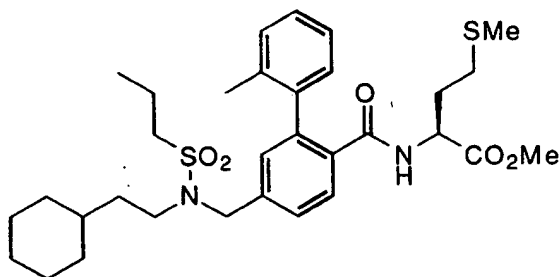


14275

Example 1187C

4-(N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl)-2-(2-methylphenyl)benzoic acid

The desired acid was prepared using the method described in Example 403E starting with the product from Example 1187B.



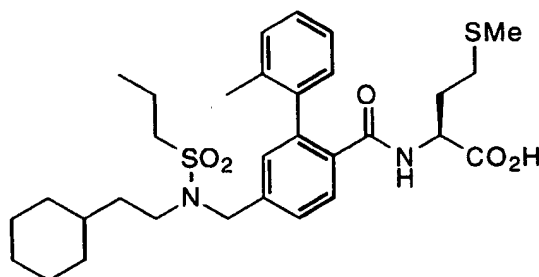
14280

Example 1187D

N-[4-N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403F starting with the product from Example 1187C. m/e (ESI) 601 (MH<sup>+</sup>)

14285

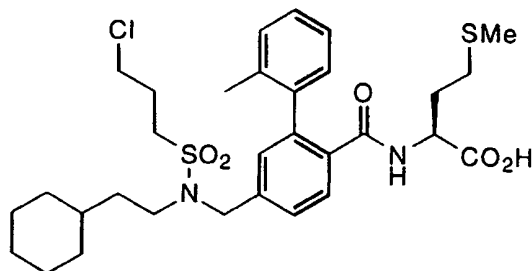
Example 1187E

N-[4-N-(2-Cyclohexylethyl)-N-propanesulfonylaminomethyl]-2-(2-methylphenyl)benzoyl]methionine

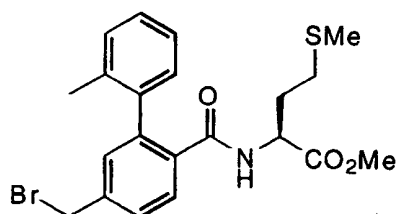
14290

The desired compound was prepared according to the method of Example 403I starting with the compound prepared in Example 1187D. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 8.00 (1H, dd, J=8&7Hz), 7.43 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.90 (1H, m), 4.58 (1H, m), 4.42 (2H, s), 3.20 (2H, m), 2.94 (2H, m), 2.20-2.00 (7H, m), 2.00-1.80 (4H,

14295 m), 1.60 (6H, m), 1.38 (2H, m), 1.15 (4H, m), 1.05 (3H, t, J=8Hz), 0.86 (2H, m). m/e  
(ESI) 587 (MH<sup>+</sup>) Anal.calc. for C<sub>31</sub>H<sub>44</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub>·0.25 H<sub>2</sub>O C 62.75, H 7.56, N 4.72  
Found C 62.75, H 7.56, N 4.49



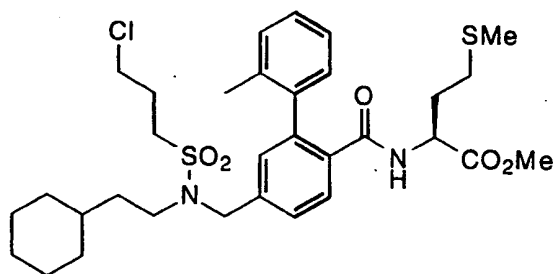
14300

Example 1188Example 1188A

14305

N-[Bromomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

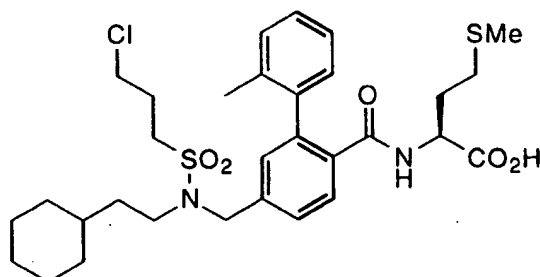
To a stirred solution at -10°C under N<sub>2</sub> of N-[4-hydroxymethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester (200 mg, 0.517 mmol), prepared as in Example 403F, and carbon tetrabromide (189 mg, 0.568 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was added triphenylphosphine (163 mg, 0.620 mmol). Reaction stirred one hour at -10°C, and  
14310 then, solvents concentrated in vacuo to produce a colorless glass. The residue could not be stored, and so, was used directly in the reaction in Example 1188B.

Example 1188B

14315

N-[4-N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

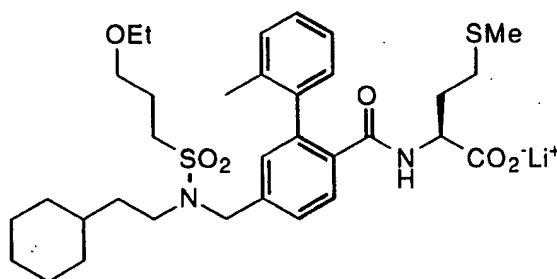
The desired compound was prepared using the method described in Example 1174B (except reaction run at  $-40^{\circ}\text{C}$ ) starting with the product from Example 1188A and N-(3-chloropropanesulfonyl)-N-(2-cyclohexylethyl)amine, prepared as in Example 1189A using the method described in Example 1174A. m/e (ESI) 635 ( $\text{MH}^-$ )



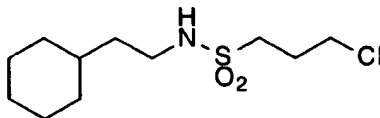
#### Example 1188C

N-[4-N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1188B.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 8.01 (1H, bt,  $J=8\text{Hz}$ ), 7.46 (1H, dd,  $J=7\&2\text{Hz}$ ), 7.40-7.10 (5H, m), 5.90 (1H, m), 4.59 (1H, m), 4.45 (2H, s), 3.68 (2H, t,  $J=8\text{Hz}$ ), 3.22 (2H, bt,  $J=7\text{Hz}$ ), 3.12 (2H, t,  $J=8\text{Hz}$ ), 2.31 (2H, m), 2.20-2.05 (4H, m), 2.03 (3H, s), 1.92 (2H, m), 1.60 (6H, m), 1.40 (2H, m), 1.30-1.00 (4H, m), 0.85 (2H, m). m/e (ESI) 621 ( $\text{MH}^-$ ) Anal. calc. for  $\text{C}_{31}\text{H}_{43}\text{Cl}_1\text{N}_2\text{O}_5\text{S}_2 \cdot 0.50 \text{H}_2\text{O}$  C 58.89, H 7.01, N 4.43 Found C 58.96, H 7.04, N 4.40



#### Example 1189

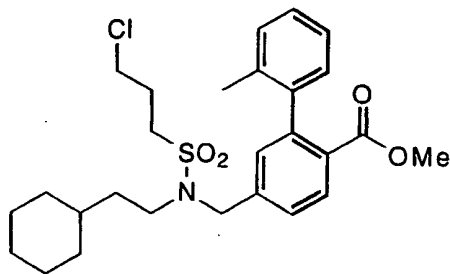


#### Example 1189A

N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)amine

14340

The desired compound was prepared using the method described in Example 1174A starting with cyclohexylethylamine and 3-chloropropanesulfonyl chloride.



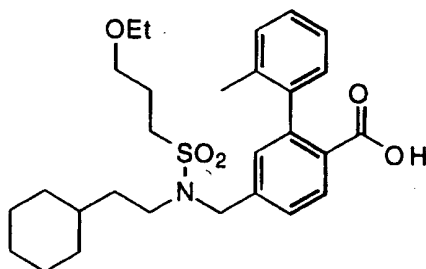
Example 1189B

14345

4-N-(3-Chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

The desired product was prepared using the method described in Example 1174B starting with the compound from Example 1189A and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D. m/e (ESI) 506 (MH<sup>+</sup>)

14350

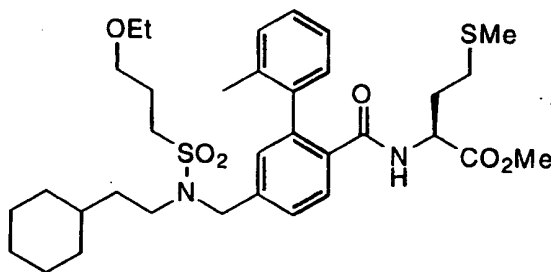


Example 1189C

N-[4-N-(2-Cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl]-2-(2-methylphenyl)benzoic acid

14355

The acid was prepared using the method described in Example 403E starting with the product from Example 1189B. Chloride was displaced by ethoxide ion.



14360

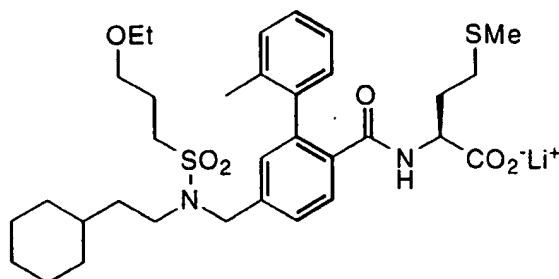
Example 1189D



N-[4-N-(2-Cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The compound was prepared using the method described in Example 403F starting with the product from Example 1189C. m/e (ESI) 645 (MH<sup>+</sup>)

14365



Example 1189E

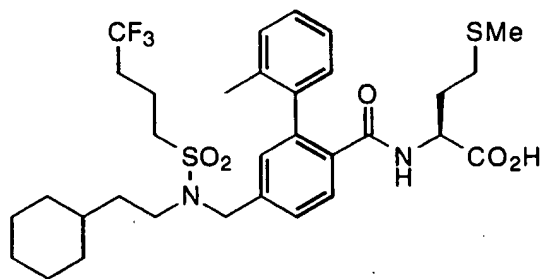
N-[4-N-(2-Cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

14370

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1189D. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.54 (1H, d, J=8Hz), 7.41 (1H, dd, J=7&2Hz), 7.30-7.10 (5H, m), 6.97 (1H, d, J=7Hz), 4.42 (2H, bs), 3.68 (1H, m), 3.43 (2H, q, J=7Hz), 3.40 (2H, m), 3.16 (4H, m), 2.20-1.95 (5H, m), 1.95 (3H, s), 1.90-1.65 (3H, m), 1.55 (6H, m), 1.27 (2H, m), 1.10 (7H, bt, J=8Hz),

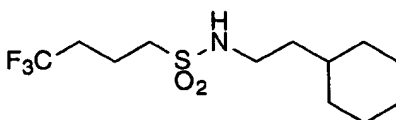
14375

0.78 (2H, m). m/e (ESI) 631 (MH<sup>+</sup>) Anal.calc. for C<sub>33</sub>H<sub>47</sub>LiN<sub>2</sub>O<sub>6</sub>S<sub>2</sub>·0.50 H<sub>2</sub>O C 61.18, H 7.47, N 4.32 Found C 61.15, H 7.53, N 4.15



14380

Example 1190

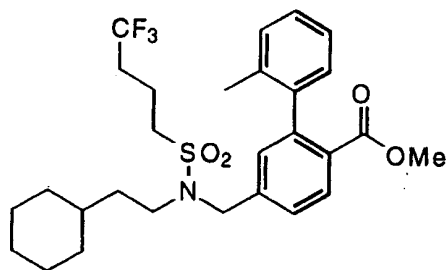


Example 1190A

N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)amine

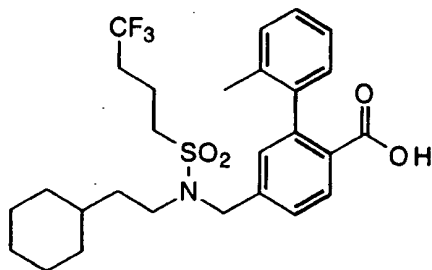
- 14385 To a stirred solution at 0°C under N<sub>2</sub> of 4,4,4-trifluoro-1-bromobutane (2.00 g, 10.5 mmol) in anhydrous DMF (10 mL) was added dropwise a slurry of t-butanethiol sodium salt (1.29 g, 11.5 mmol) in anhydrous DMF (25 mL) such that the temperature was maintained below 5°C. Mixture stirred one hour at 0°C, and then, diluted with water and extracted with ether. Extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo.
- 14390 Residue dissolved in 1:1 water/EtOH at 0°C, and to this was bubbled in chlorine gas for 45 minutes. After the chlorine addition, N<sub>2</sub> was bubbled into the black-green mixture until the green color disappeared (30 minutes). The mixture was made a more homogeneous solution by addition of CH<sub>2</sub>Cl<sub>2</sub>, and to this was added carefully an aqueous 2M Na<sub>2</sub>CO<sub>3</sub> solution until mixture was basic (pH 10). Cyclohexylethylamine (1.14 g, 9.00 mmol) was added,
- 14395 and this two-phase solution was stirred at room temperature overnight. Reaction diluted with water and extracted with CHCl<sub>3</sub> (2x). Extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. Residue purified by flash chromatography on silica gel eluting with 20% EtOAc/Hexanes to afford the desired product as a light brown oil (1.02 g, 32%). m/e (DCI) 319 (MH+NH<sub>3</sub><sup>+</sup>)

14400

Example 1190B4-(N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

14405

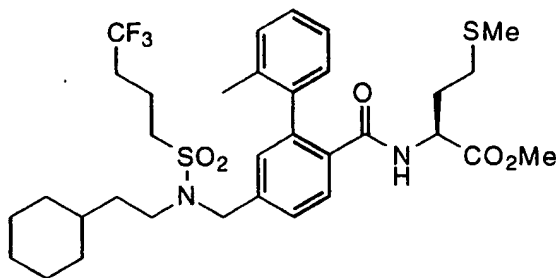
The desired product was prepared using the method described in Example 1174B starting with N-(2-cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)amine, prepared as in Example 1190A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D.



14410

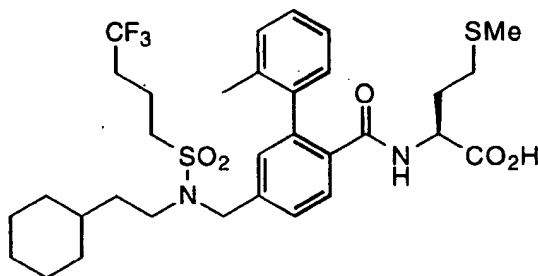
Example 1190C4-(N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

14415 The desired acid was prepared using the method described in Example 403E starting with the product from Example 1190B. m/e (ESI) 524 (MH<sup>-</sup>)

Example 1190DN-[4-N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

14420

The desired compound was prepared using the method described in Example 403F starting with the product from Example 1190C. m/e (ESI) 669 (MH<sup>-</sup>)



14425

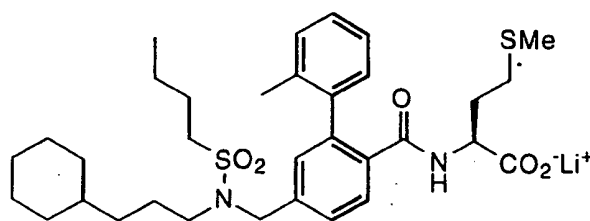
Example 1190EN-[4-N-(2-Cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1190D. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) (rotamer)

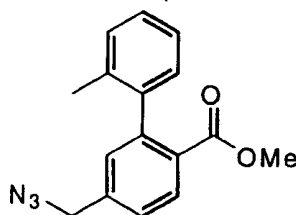
14430

8.01(7.98) (1H, d, J=8Hz), 7.46 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.92 (1H, m), 4.80 (1H, bs), 4.58 (1H, m), 4.45 (2H, s), 3.22 (2H, bt, J=7Hz), 3.03 (2H, t, J=8Hz), 2.30 (2H, m), 2.20-2.00 (10H, m), 1.92 (1H, m), 1.62 (6H, m), 1.40 (2H, m), 1.30-1.00 (4H, m), 0.87 (2H, m). m/e (ESI) 655 (MH<sup>-</sup>) Anal.calc. for C<sub>32</sub>H<sub>43</sub>F<sub>3</sub>N<sub>2</sub>O<sub>5</sub>S<sub>2</sub> C 58.52, H 6.60, N 4.26 Found C 58.27, H 6.63, N 4.13

14435

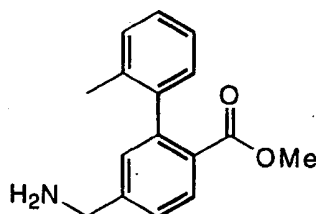
Example 1191

14440

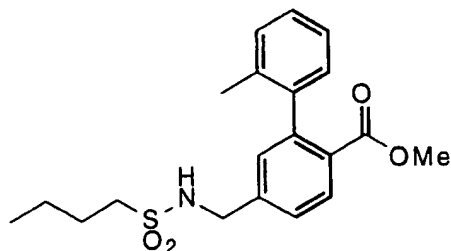
Example 1191A4-Azidomethyl-2-(2-methylphenyl)benzoic acid methyl ester

To a stirred mixture at 0°C under N<sub>2</sub> of sodium azide (1.47 g, 22.6 mmol) in anhydrous DMF (30 mL) was added a solution of 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester (6.00 g, 18.8 mmol), prepared as in Example 1178A-D, in anhydrous DMF (10 mL). Reaction stirred overnight at room temperature. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo.

14450

Example 1191B4-Aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

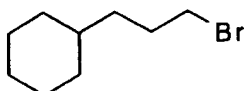
To a flask at ambient temperature under N<sub>2</sub> containing 10% palladium on carbon catalyst (1.0 g) was added a solution of 4-azidomethyl-2-(2-methylphenyl)benzoic acid methyl ester (5.00 g, 17.8 mmol), prepared as in Example 1191A, in MeOH (75 mL). Two drops of conc. HCl added, and reaction stirred vigorously overnight under an atmosphere of H<sub>2</sub>. Catalyst filtered off through celite and washed with MeOH. Filtrate concentrated in vacuo, and residue taken up in an aqueous 4N NaOH solution. Aqueous solution extracted with CHCl<sub>3</sub> (3x), and extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo to afford the desired product (1.37 g, 30%). m/e (DCI) 256 (MH<sup>+</sup>)

Example 1191C

14465

4-N-Butanesulfonylaminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

The desired compound was prepared using the method described in Example 1174A starting with 4-aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1191B, and butanesulfonyl chloride. m/e (ESI) 374 (MH<sup>+</sup>)



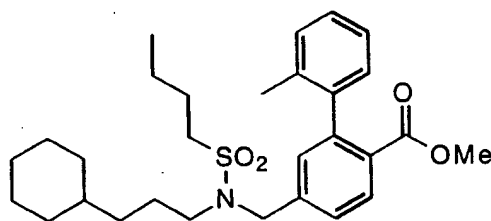
14470

Example 1191D1-Bromo-3-cyclohexylpropane

The desired compound was prepared according to the method of Example 1178D starting with 3-cyclohexyl-1-propanol. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 3.40 (2H, t, J=8Hz),

14475

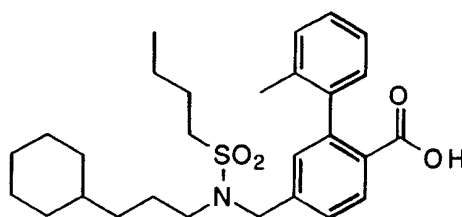
1.85 (2H, m), 1.80-1.50 (6H, m), 1.40-1.10 (5H, m), 0.90 (2H, m).

Example 1191EN-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl]-2-(2-methylphenyl)benzoic acid methyl ester

14480

The desired compound was prepared using the method described in Example 1174B starting with the compounds from Example 1191C and Example 1191D. m/e (ESI) 500 (MH<sup>+</sup>)

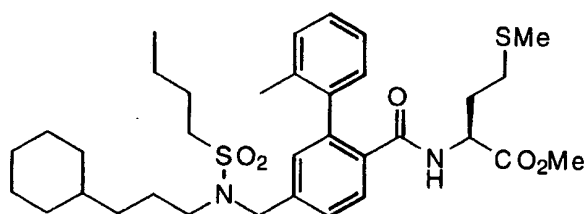
14485

Example 1191F

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl]-2-(2-methylphenyl)benzoic acid

14490

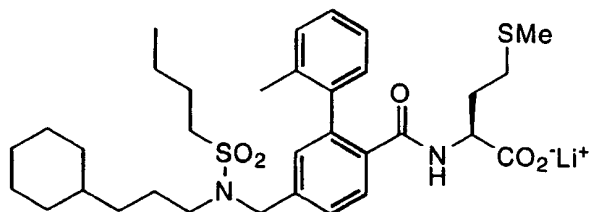
The acid was prepared using the method described in Example 403E starting with the compound from Example 1191E.

Example 1191G

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

14495

The compound was prepared using the method described in Example 403F starting with the compound from Example 1191F. m/e (ESI) 629 (MH<sup>-</sup>)



14500

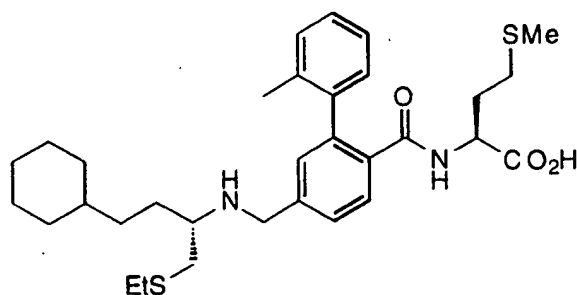
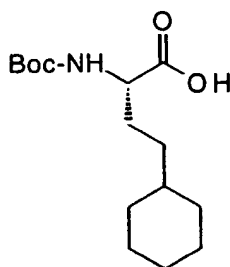
Example 1191H

N-[4-N-(Butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

14505

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1191G. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.54 (1H, d, J=8Hz), 7.41 (1H, bd, J=7Hz), 7.30-7.05 (5H, m), 6.97 (1H, d, J=7Hz), 4.42 (2H, s), 3.68 (1H, m), 3.10 (4H, bt, J=7Hz), 2.20-1.95 (5H, m), 1.91 (3H, s), 1.90-1.45 (9H, m), 1.45-1.20 (4H, m), 1.20-0.90 (6H, m), 0.88 (3H, t, J=8Hz), 0.73 (2H, m). m/e (ESI) 615 (MH<sup>-</sup>) Anal.calc. for C<sub>33</sub>H<sub>47</sub>LiN<sub>2</sub>O<sub>5</sub>S<sub>2</sub>·0.75 H<sub>2</sub>O C 62.29, H 7.68, N 4.40 Found C 62.18, H 7.75, N 4.36

14510

Example 1193

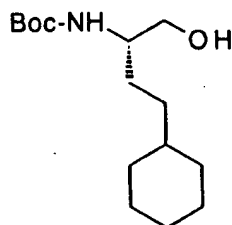
14515

Example 1193A(2S)-t-Butoxycarbonylamino-4-cyclohexylbutanoic acid

To a solution of Boc-homophenylalanine (3.00 g, 10.8 mmol) in  $\text{CH}_2\text{Cl}_2$  at room temperature was added a solution of 4N HCl in dioxane (20 mL, 80 mmol), and mixture stirred overnight. Solvents concentrated, and white powder that resulted was reduced under high pressure (4 atm.  $\text{H}_2$ ) using platinum/HCl. The white solid that resulted from the reduction was mixed with aqueous 4N NaOH (30 mL), water (30 mL), and THF (50 mL) at room temperature, and to this was added di-t-butyl dicarbonate (3.5 g, 16 mmol). Reaction heated at  $70^\circ\text{C}$  overnight. Reaction cooled to  $0^\circ\text{C}$ , and an aqueous solution of 3N HCl added until the pH reached 6. Product extracted out with  $\text{CHCl}_3$ , and extracts dried with  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo to produce a white solid (3.24 g, 106%). m/e (DCI) 286 ( $\text{MH}^+$ )

14520

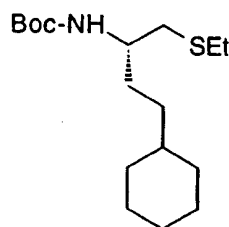
14525



14530

Example 1193B(2S)-t-Butoxycarbonylamino-4-cyclohexylbutan-1-ol

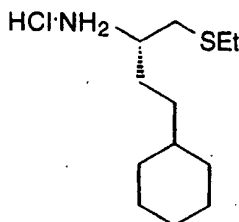
To a solution at -5°C under N<sub>2</sub> of (2S)-t-butoxycarbonylamino-4-cyclohexylbutanoic acid (3.24 g, 10.8 mmol), prepared as in Example 1193A, in anhydrous THF (20 mL) was added dropwise a 1.0M borane-THF complex (32.3 mL, 32.3 mmol) in THF. After addition, reaction stirred overnight at room temperature. Reaction cooled to 0°C and quenched with an aqueous 4N NaOH solution. Stirred 30 minutes at room temperature, and then, extracted with CH<sub>2</sub>Cl<sub>2</sub> (3x). Extracts dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 30% EtOAc/Hexanes to afford the desired product as a colorless oil (696 mg, 23%). m/e (DCI) 272 (MH<sup>+</sup>)



### Example 1193C

(2S)-t-Butoxycarbonylamino-4-cyclohexyl-1-ethylthiobutane

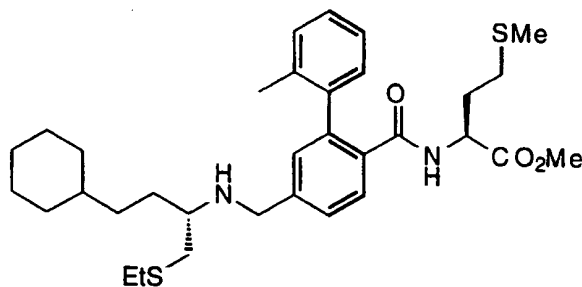
14545 The desired compound was prepared using the method described in Example 403B and 403C starting with the product from Example 1193B. m/e (DCI) 316 (MH<sup>+</sup>)



Example 1193D

(2S)-Amino-4-cyclohexyl-1-ethylthiobutane hydrochloride salt

The desired compound was prepared using the method described in Example 403D starting with the product from Example 1193C.





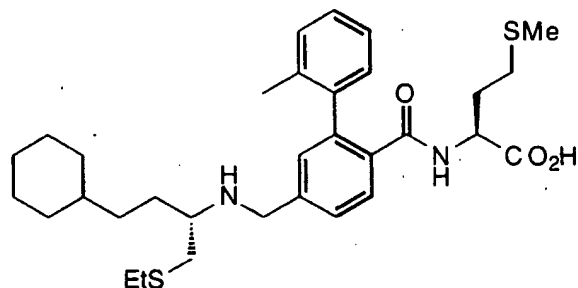
14555

Example 1193E

N-[4-N-(4-Cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with the product from Example 1193D and N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G. m/e (ESI) 585 (MH<sup>+</sup>)

14560

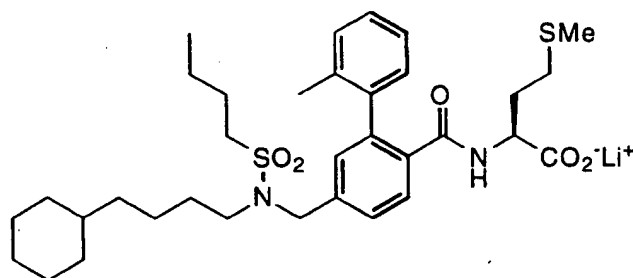
Example 1193F

14565

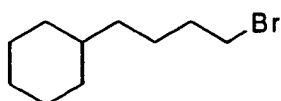
N-[4-N-(4-Cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1193E. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.72 (1H, m), 7.45 (1H, m), 7.40-7.00 (5H, m), 6.18 (1H, m), 4.36 (1H, m), 4.00 (2H, m), 2.95 (1H, m), 2.82 (1H, m), 2.73 (1H, m), 2.44 (2H, m), 2.20-2.00 (7H, m), 1.98 (3H, bs), 1.90-1.40 (7H, m), 1.20 (9H, t, J=8Hz), 0.87 (3H, m). m/e (ESI) 569 (MH<sup>+</sup>) Anal. calc. for C<sub>32</sub>H<sub>46</sub>N<sub>2</sub>O<sub>3</sub>S<sub>2</sub>·0.75 H<sub>2</sub>O C 65.77, H 8.19, N 4.79 Found C 65.74, H 8.08, N 4.69

14570



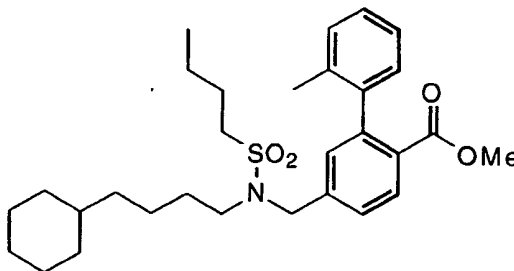
14575

Example 1194Example 1194A

14580

1-Bromo-4-cyclohexylbutane

The desired compound was prepared according to the method of Example 1178D starting with 4-cyclohexyl-1-butanol.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 3.40 (2H, t,  $J=8\text{Hz}$ ), 1.83 (2H, m), 1.80-1.50 (6H, m), 1.42 (2H, m), 1.30-1.10 (5H, m), 0.85 (2H, m).

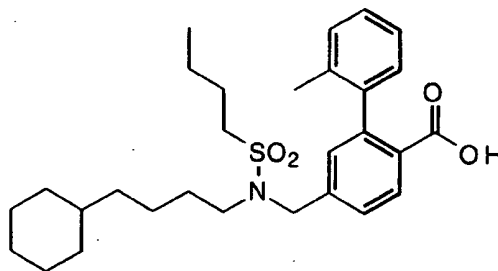


14585

Example 1194B

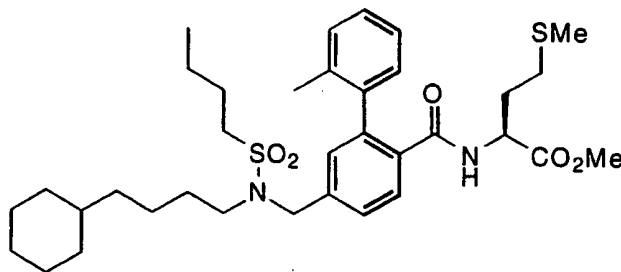
4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

The desired compound was prepared using the method described in Example 1174B starting with the compounds from Example 1191C and Example 1194A. m/e (ESI) 514 ( $\text{MH}^+$ )

Example 1194C

4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoic acid

The acid was prepared using the method described in Example 403E starting with the compound from Example 1194B.

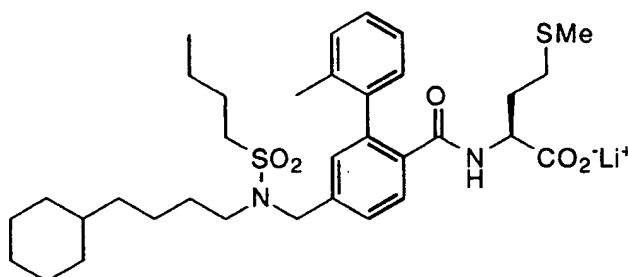


14600

Example 1194D

N-[4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

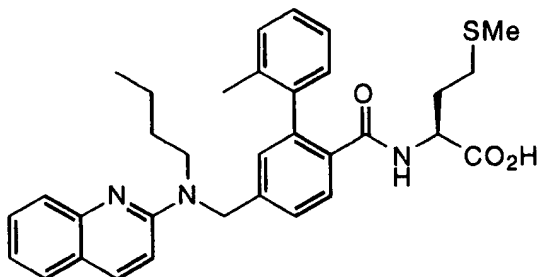
The compound was prepared using the method described in Example 403F starting with the compound from Example 1194C. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.96 (1H, m), 7.43 (1H, dd, J=7&2Hz), 7.40-7.10 (5H, m), 5.90 (1H, bd, J=7Hz), 4.62 (1H, m), 4.44 (2H, s), 3.64 (3H, s), 3.18 (2H, m), 2.96 (2H, m), 2.20-1.85 (8H, m), 1.75-1.50 (9H, m), 1.50-1.30 (4H, m), 1.25-1.00 (8H, m), 0.94 (3H, t, J=8Hz), 0.82 (2H, m).



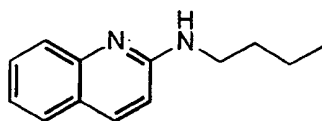
Example 1194E

N-[4-N-(Butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1194D. <sup>1</sup>H (300MHz, DMSO-d<sub>6</sub>, δ) 7.56 (1H, d, J=8Hz), 7.41 (1H, dd, J=7&2Hz), 7.30-7.05 (5H, m), 6.98 (1H, d, J=7Hz), 4.42 (2H, bs), 3.68 (1H, m), 3.13 (4H, m), 2.20-1.95 (5H, m), 1.92 (3H, s), 1.90-1.45 (9H, m), 1.45-1.20 (4H, m), 1.20-0.90 (8H, m), 0.88 (3H, t, J=8Hz), 0.78 (2H, m). m/e (ESI) 629 (MH<sup>+</sup>) Anal. calc. for C<sub>34</sub>H<sub>49</sub>LiN<sub>2</sub>O<sub>5</sub>S<sub>2</sub>·0.75 H<sub>2</sub>O C 62.79, H 7.83, N 4.31 Found C 62.69, H 7.84, N 4.24



Example 1195

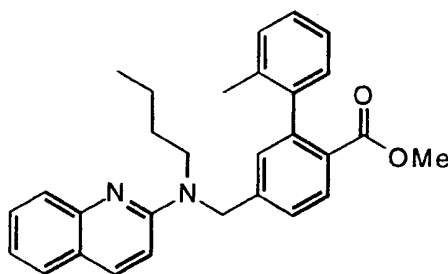


Example 1195A

N-Butyl-N-quinolin-2-ylamine

14630 2-Chloroquinoline (500 mg, 3.06 mmol), butylamine (0.90 mL, 9.16 mmol), and diisopropylethylamine (0.82 mL, 4.58 mmol) were dissolved in acetonitrile (5 mL), and solution refluxed 2 days. Reaction cooled and diluted with EtOAc. Reaction washed with water and brine. Organic layer dried with Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting with 15% EtOAc/Hexanes to afford the desired product as a pale yellow oil (188 mg, 31%). m/e (DCI) 201 (MH<sup>+</sup>)

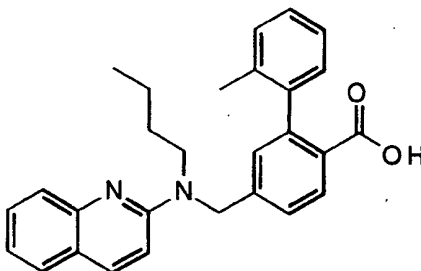
14635



Example 1195B

4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

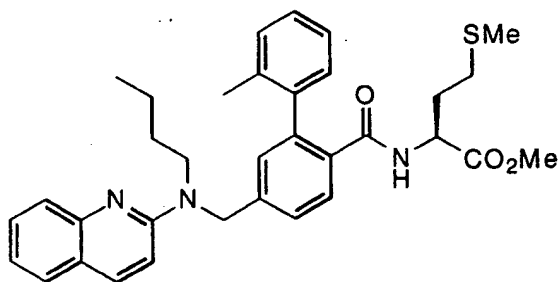
14640 The desired compound was prepared according to the method of Example 1174B starting with 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D, and the compound from Example 1195A.



Example 1195C

4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoic acid

14645 The desired acid was prepared using the method described in Example 403E starting with the product from Example 1195B.



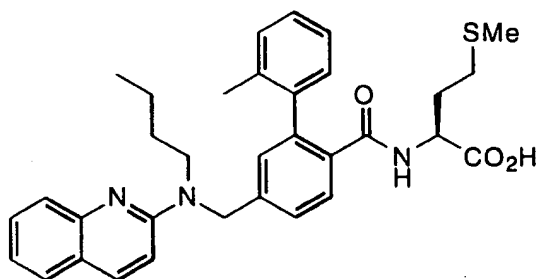
14650

Example 1195D

N-[4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403F starting with the product from Example 1195C. m/e (ESI) 570 (MH<sup>+</sup>)

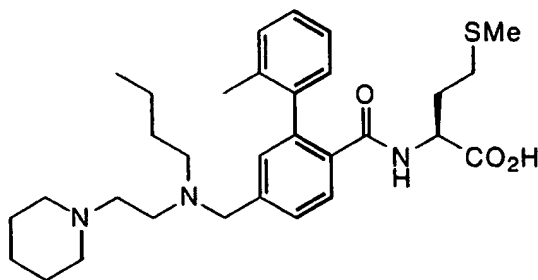
14655

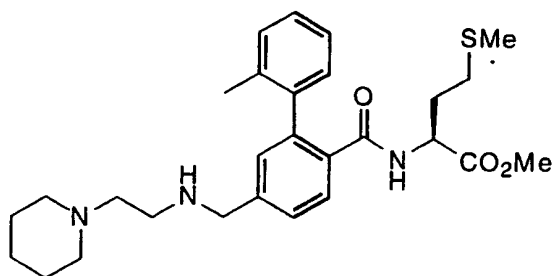
Example 1195E

N-[4-N-Butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1195D. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.95-7.80 (3H, m), 7.72 (1H, m), 7.60-7.40 (2H, m), 7.37 (1H, dd, J=7&2Hz), 7.30-7.00 (5H, m), 6.84 (1H, d, J=9Hz), 6.03 (1H, m), 5.03 (2H, bs), 4.44 (1H, m), 3.62 (2H, m), 2.20-2.00 (5H, m), 1.96 (3H, s), 1.85 (1H, m), 1.65 (2H, m), 1.51 (1H, m), 1.37 (2H, m), 0.93 (3H, t, J=8Hz). m/e (ESI) 554 (MH<sup>-</sup>) Anal.calc. for C<sub>33</sub>H<sub>37</sub>N<sub>3</sub>O<sub>3</sub>S·0.40 H<sub>2</sub>O C 70.41, H 6.77, N 7.46 Found C 70.62, H 6.68, N 7.07

14665

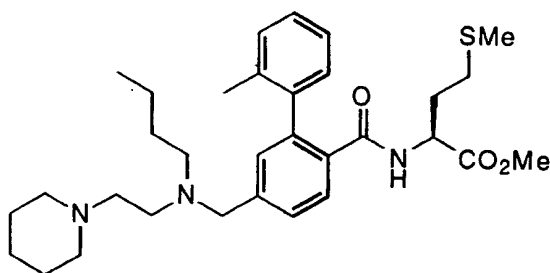
Example 1196



14670

Example 1196AN-[4-(N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

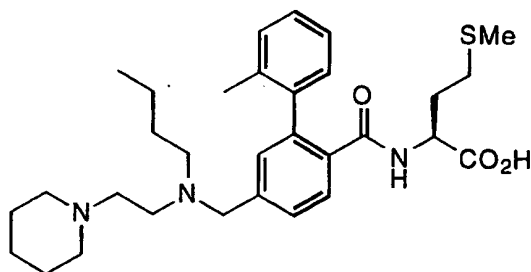
14675 The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 1-(2-aminoethyl)piperidine. m/e (ESI) 498 (MH<sup>+</sup>)

Example 1196B

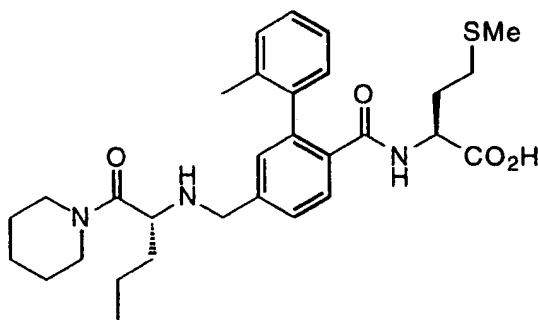
14680 N-[4-(N-Butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1196A and butyraldehyde. m/e (ESI) 552 (MH<sup>+</sup>)

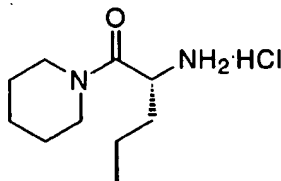
14685

Example 1196CN-[4-(N-Butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine

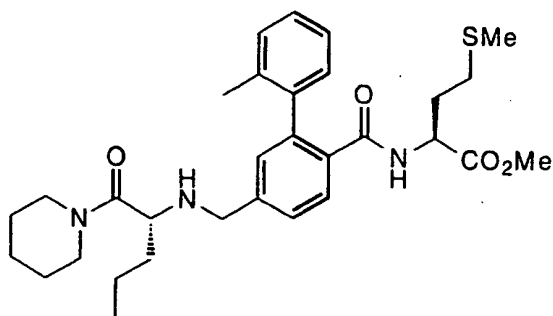
- 14690 The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1196B.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.62 (1H, d,  $J=8\text{Hz}$ ), 7.30-7.10 (5H, m), 7.09 (1H, bs), 6.42 (1H, m), 4.35 (1H, m), 3.63 (2H, m), 3.05-2.75 (8H, m), 2.42 (2H, bt,  $J=7\text{Hz}$ ), 2.20-1.90 (9H, m), 1.90-1.60 (5H, m), 1.55 (2H, m), 1.40 (2H, m), 1.22 (2H, m), 0.83 (3H, t,  $J=8\text{Hz}$ ).  $m/e$  (ESI) 538 ( $\text{MH}^+$ )
- 14695 Anal. calc. for  $\text{C}_{31}\text{H}_{45}\text{N}_3\text{O}_3\text{S}\cdot 0.75\text{H}_2\text{O}$  C 67.30, H 8.47, N 7.59 Found C 67.21, H 8.39, N 7.52



14700

Example 1197Example 1197AN-(1-Morpholinocarbonyl)butylamine hydrochloride salt

- 14705 To a stirred solution at room temperature of Boc-L-norvaline (500 mg, 2.30 mmol) and piperidine (0.27 mL, 2.76 mmol) in DMF (5 mL) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (530 mg, 2.76 mmol). Reaction stirred overnight at room temperature. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. Residue mixed with a 4N
- 14710 HCl solution (10 mL, 40 mmol) in dioxane at room temperature overnight. Solvents concentrated in vacuo to afford the desired compound (222 mg, 44%).  $m/e$  (DCI) 185 ( $\text{MH}^+$ )

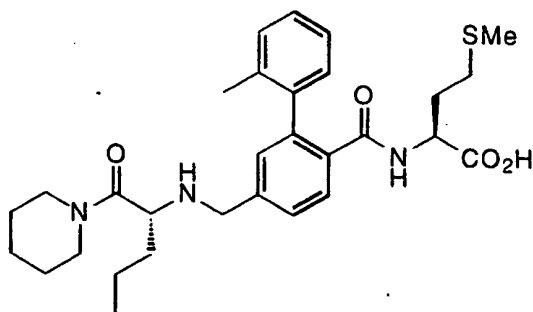


14715

Example 1197BN-[4-N-((1-Morpholinocarbonyl)butyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and the compound prepared in Example 1197A. m/e (ESI) 554 (MH<sup>+</sup>)

14720

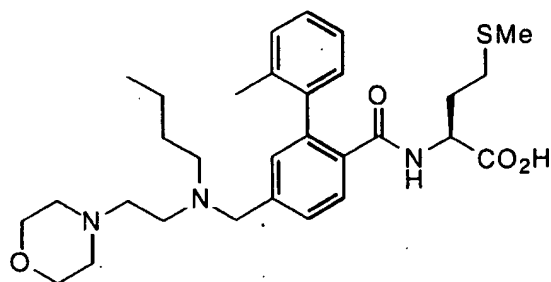
Example 1197CN-[4-N-((1-Morpholinocarbonyl)butyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

14725

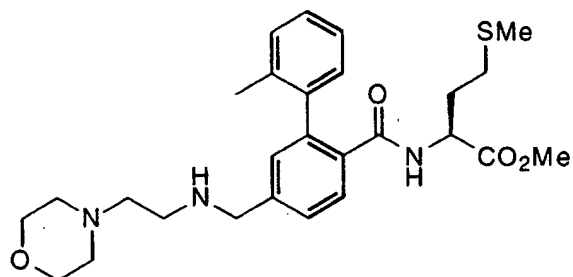
The desired compound was prepared using the method described in Example 403I starting with the compound from Example 1197B. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.82 (1H, m), 7.43 (1H, dd, J=7&2Hz), 7.40-7.20 (4H, m), 7.17 (1H, d, J=2Hz), 6.08 (1H, m), 5.97 (1H, m), 4.43 (1H, m), 4.20-3.80 (2H, m), 3.69 (2H, m), 3.60-3.30 (3H, m), 2.20-1.90 (8H, m), 1.91 (2H, m), 1.66 (4H, m), 1.57 (4H, m), 1.30 (2H, m), 0.89 (3H, t, J=8Hz). m/e (ESI) 538 (MH<sup>+</sup>) Anal. calc. for C<sub>30</sub>H<sub>41</sub>N<sub>3</sub>O<sub>4</sub>S·0.75 H<sub>2</sub>O C 65.13, H 7.74, N 7.59 Found C 65.40, H 7.44, N 7.26

14730





14735

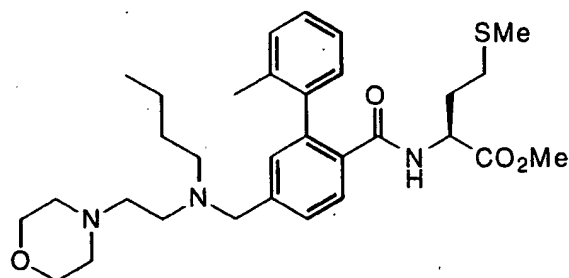
Example 1198Example 1198A

14740

N-[4-(N-(2-Morpholin-4-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 4-(2-aminoethyl)morpholine. m/e (ESI) 500 (MH<sup>+</sup>)

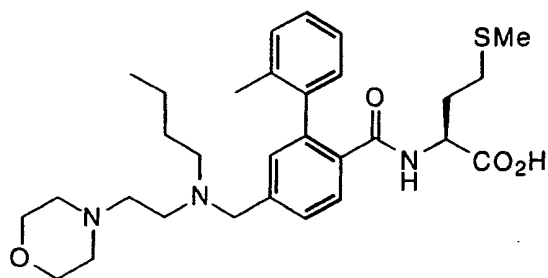
14745

Example 1198B

N-[4-N-Butyl-N-(2-morpholin-4-ylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

14750

The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1198A and butyraldehyde. m/e (ESI) 554 (MH<sup>+</sup>)

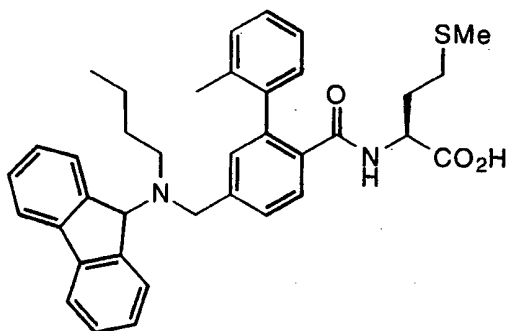
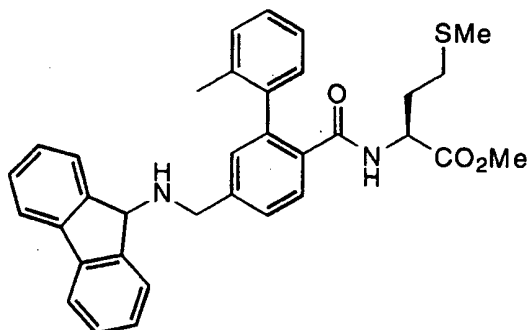


14755

Example 1198CN-[4-N-Butyl-N-(2-morpholin-4-ylethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1198B. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.71 (1H, d, J=9Hz), 7.43 (1H, bd, J=8Hz), 7.30-7.10 (5H, m), 6.25 (1H, m), 4.39 (1H, m), 3.83 (2H, bs), 3.72 (4H, m), 2.89 (2H, m), 2.80-2.50 (8H, m), 2.20-1.80 (9H, m), 1.62 (1H, m), 1.50 (2H, m), 1.27 (2H, m), 0.88 (3H, t, J=8Hz). m/e (ESI) 540 (MH<sup>+</sup>) Anal. calc. for C<sub>30</sub>H<sub>43</sub>N<sub>3</sub>O<sub>4</sub>S·0.50 H<sub>2</sub>O C 65.42, H 8.05, N 7.63 Found C 65.22, H 7.92, N 7.47

14765

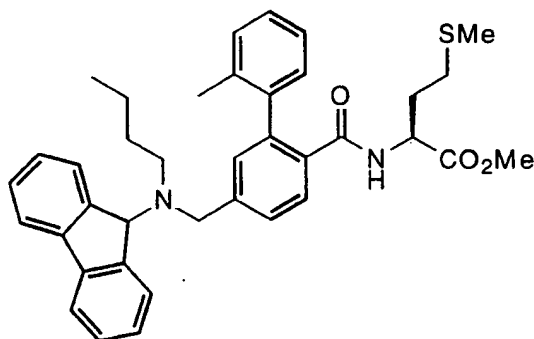
Example 1199

14770

Example 1199AN-[4-(N-(9-fluorenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 9-aminofluorene hydrochloride salt m/e (ESI) 551 (MH<sup>+</sup>)

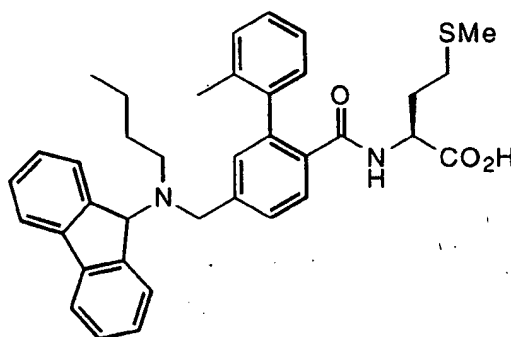
14775

Example 1199B

N-[4-N-Butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

14780

The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1199A and butyraldehyde. m/e (ESI) 605 (MH<sup>-</sup>)



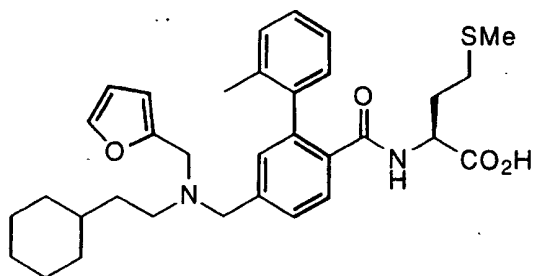
14785

Example 1199C

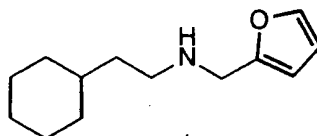
N-[4-N-Butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

14790

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1199B. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.91 (1H, m), 7.67 (3H, m), 7.47 (1H, bd, J=8Hz), 7.40-7.10 (10H, m), 5.84 (1H, m), 5.00 (1H, bs), 4.52 (1H, m), 3.53 (2H, bs), 2.64 (2H, m), 2.20-1.95 (8H, m), 1.90 (1H, m), 1.52 (3H, m), 1.32 (2H, m), 0.83 (3H, bt, J=8Hz). m/e (ESI) 591 (MH<sup>-</sup>) Anal.calc. for C<sub>37</sub>H<sub>40</sub>N<sub>2</sub>O<sub>3</sub>S·0.50 H<sub>2</sub>O C 73.85, H 6.87, N 4.65 Found C 74.07, H 6.70, N 4.63



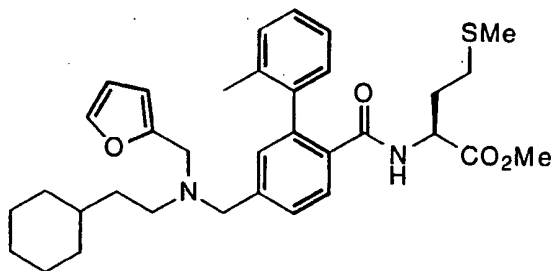
14795

Example 1200

14800

Example 1200AN-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)amine

The desired amine was prepared using the method described in Example 1171A starting with cyclohexylethylamine and 2-furoic acid. m/e (DCI/NH<sub>3</sub>) 208 (MH<sup>+</sup>)

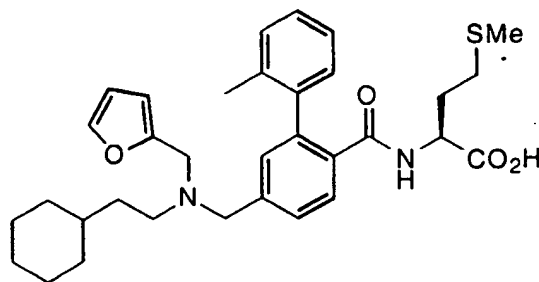


14805

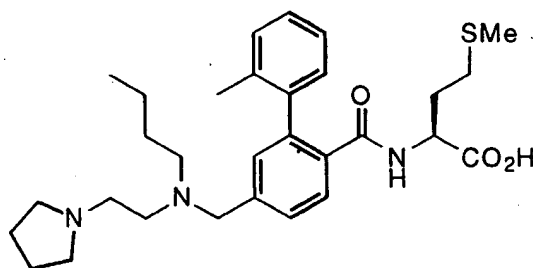
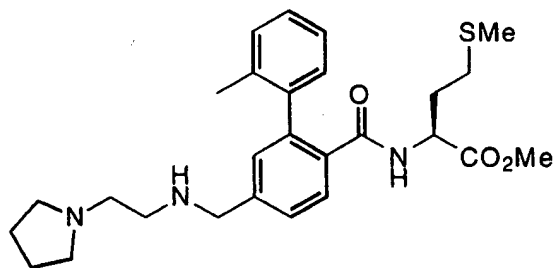
Example 1200B

N-[4-N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

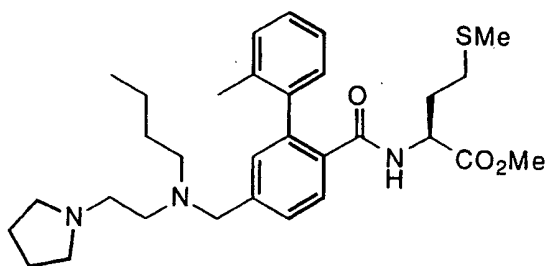
14810 The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)amine, prepared as in Example 1200A. m/e (ESI) 577 (MH<sup>+</sup>)

Example 1200CN-[4-N-(2-Cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1200B.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 7.81 (1H, d,  $J=8\text{Hz}$ ), 7.56 (1H, m), 7.42 (1H, d,  $J=2\text{Hz}$ ), 7.30-7.10 (5H, m), 6.37 (2H, bs), 6.15 (1H, d,  $J=8\text{Hz}$ ), 4.45 (1H, m), 4.10-3.80 (4H, m), 2.67 (2H, m), 2.20-2.05 (5H, m), 2.00 (3H, s), 1.90 (1H, m), 1.80-1.40 (8H, m), 1.30-1.00 (4H, m), 0.88 (2H, m). m/e (ESI) 561 ( $\text{MH}^+$ ) Anal.calc. for  $\text{C}_{33}\text{H}_{42}\text{N}_2\text{O}_4\text{S} \cdot 1.00 \text{ H}_2\text{O}$  C 68.25, H 7.64, N 4.82 Found C 67.94, H 7.34, N 4.65

Example 1201Example 1201AN-[4-(N-(2-Pyrrolidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

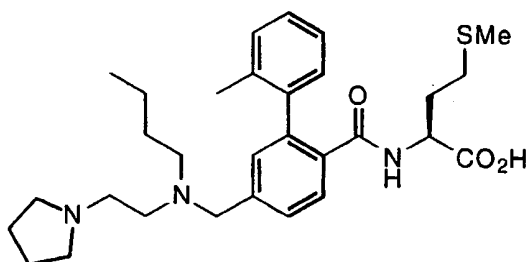
The desired compound was prepared using the method described in Example 403H starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 1-(2-aminoethyl)pyrrolidine. m/e (ESI) 484 (MH<sup>+</sup>)



#### Example 1201B

N-[4-N-Butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with the compound prepared in Example 1201A and butyraldehyde. m/e (ESI) 540 (MH<sup>+</sup>)

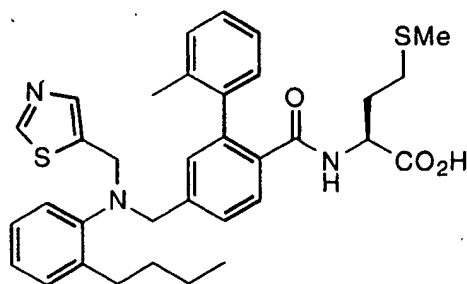


#### Example 1201C

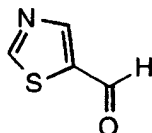
N-[4-N-Butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1201B. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.66 (1H, d, J=8Hz), 7.35-7.10 (5H, m), 7.09 (1H, bs), 6.37 (1H, m), 4.36 (1H, m), 3.63 (2H, s), 3.16 (4H, m), 3.03 (2H, m), 2.84 (2H, m), 2.43 (2H, bt, J=8Hz), 2.20-1.80 (13H, m), 1.65 (1H, m), 1.41 (2H, m), 1.23 (2H, m), 0.85 (3H, t, J=8Hz). m/e (ESI) 524 (MH<sup>+</sup>)

Anal.calc. for C<sub>30</sub>H<sub>43</sub>N<sub>3</sub>O<sub>3</sub>S·1.00 H<sub>2</sub>O C 66.27, H 8.34, N 7.73 Found C 65.92, H 8.29, N 7.59

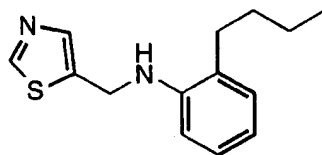


14860

Example 1202Example 1202A5-Thiazolecarboxaldehyde

14865

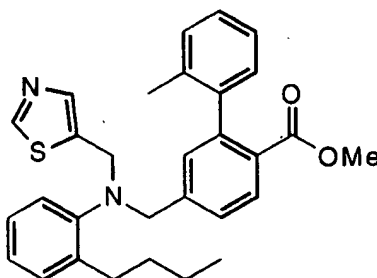
The desired compound was prepared according to the method of Example 403G starting with 5-hydroxymethylthiazole.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 10.13 (1H, s), 9.12 (1H, s), 8.54 (1H, s).



14870

Example 1202BN-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)amine

The desired compound was prepared according to the method of Example 403H starting with 2-butylaniline and the aldehyde from Example 1202A.  $m/e$  (DCI) 247 ( $\text{MH}^+$ )

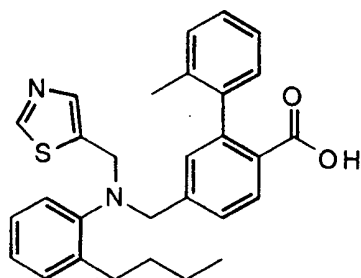


14875

Example 1202C

4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoic acid methyl ester

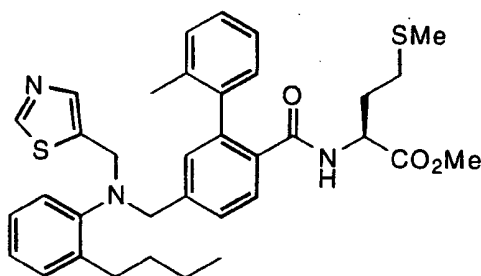
The desired compound was prepared according to the method of Example 1174B  
 14880 starting with 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in  
 Example 1178A-D, and the compound from Example 1202B.



Example 1202D

14885 4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoic acid

The desired acid was prepared using the method described in Example 403E starting  
 with the product from Example 1202C.

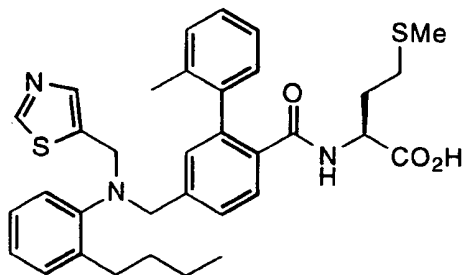


Example 1202E

14890 N-[4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403F  
 starting with the product from Example 1202D. m/e (ESI) 614 (MH<sup>+</sup>)

14895

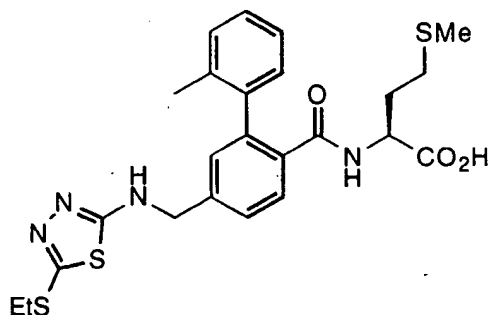


Example 1202F

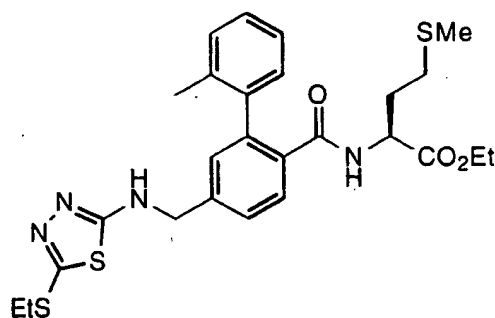
N-[4-N-(2-Butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine



- 14900 The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1202E.  $^1\text{H}$  (300MHz,  $\text{CDCl}_3$ ,  $\delta$ ) 8.73 (1H, s), 7.91 (1H, bt,  $J=8\text{Hz}$ ), 7.66 (1H, bs), 7.40-7.15 (5H, m), 7.15-6.90 (5H, bs), 5.88 (1H, d,  $J=8\text{Hz}$ ), 4.57 (1H, m), 4.29 (2H, s), 4.13 (2H, s), 2.72 (2H, bt,  $J=8\text{Hz}$ ), 2.20-1.80 (9H, m), 1.55 (3H, m), 1.35 (2H, m), 0.88 (3H, t,  $J=8\text{Hz}$ ).  $m/e$  (ESI) 600 ( $\text{MH}^+$ )
- 14905 Anal.calc. for  $\text{C}_{34}\text{H}_{39}\text{N}_3\text{O}_3\text{S}_2$  C 67.86, H 6.53, N 6.98 Found C 67.57, H 6.43, N 6.71

Example 1203

14910

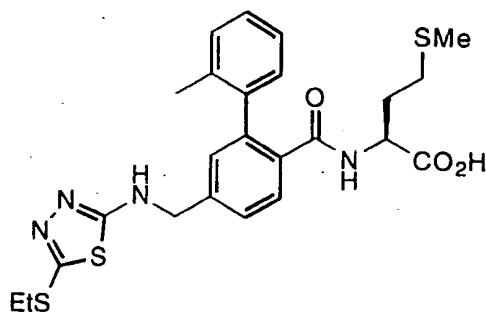
Example 1203A

N-[4-N-((2-Ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine ethyl ester

- 14915 2-Amino-5-(ethylthio)-1,3,4-thiadiazole (419 mg, 2.60 mmol) and N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester (1.00 g, 2.60 mmol), prepared as in Example 403G, were mixed with toluene (4 mL) and refluxed under  $\text{N}_2$  with a Dean-Stark trap overnight. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. To a solution of this
- 14920 residue in EtOH (8 mL) at  $0^\circ\text{C}$  under  $\text{N}_2$  was added sodium borohydride (98 mg, 2.60 mmol), and mixture stirred vigorously at ambient temperature for 3 hours. Reaction diluted with EtOAc and washed with water and brine. Organic layer dried with  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. Residue purified by flash chromatography on silica gel eluting

with 60% EtOAc/Hexanes to afford the desired product as a pale yellow oil (347 mg, 25%).

14925 m/e (ESI) 543 (MH<sup>+</sup>)



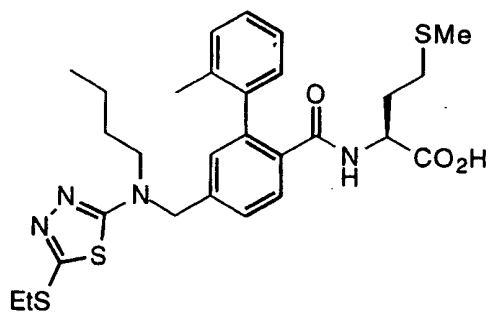
#### Example 1203B

N-[4-N-((2-Ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

14930

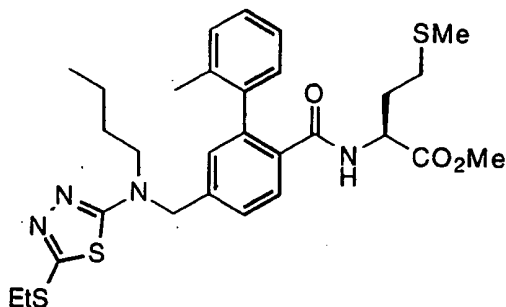
The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1203A. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.88 (1H, m), 7.46 (1H, m), 7.30-7.00 (5H, m), 5.94 (2H, m), 4.58 (1H, m), 4.42 (2H, bd, J=8Hz), 3.13 (2H, q, J=8Hz), 2.20-1.80 (9H, m), 1.67 (1H, m), 1.39 (3H, t, J=8Hz). m/e (ESI) 515 (MH<sup>+</sup>) Anal.calc. for C<sub>24</sub>H<sub>28</sub>N<sub>4</sub>O<sub>3</sub>S<sub>3</sub>·0.50 H<sub>2</sub>O C 54.83, H 5.56, N 10.66 Found C 54.86, H 5.41, N 11.04

14935



14940

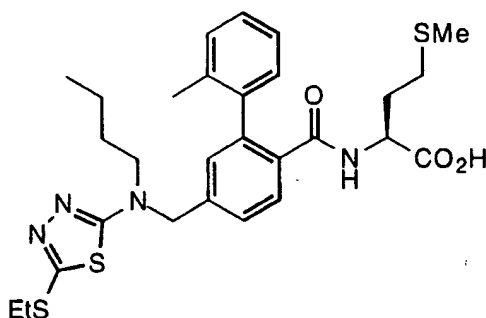
#### Example 1204



Example 1204A

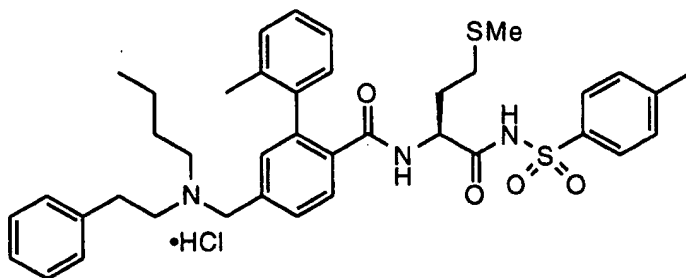
N-[4-N-Butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared using the method described in Example 403H starting with the compound prepared as in Example 1203A (methyl ester) and butyraldehyde. m/e (ESI) 587 (MH<sup>+</sup>)

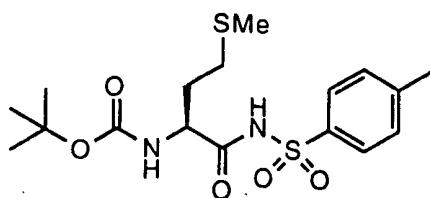
Example 1204B

N-[4-N-Butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with the compound from Example 1204A. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.81 (1H, m), 7.43 (1H, bd, J=8Hz), 7.30-7.10 (5H, m), 6.00 (1H, d, J=8Hz), 5.38 (2H, m), 4.48 (1H, m), 3.17 (2H, m), 3.02 (2H, q, J=8Hz), 2.20-1.80 (9H, m), 1.60 (3H, m), 1.32 (5H, t, J=8Hz), 0.88 (3H, t, J=8Hz). m/e (ESI) 571 (MH<sup>+</sup>) Anal.calc. for C<sub>28</sub>H<sub>36</sub>N<sub>4</sub>O<sub>3</sub>S<sub>3</sub>·0.50 H<sub>2</sub>O C 57.80, H 6.41, N 9.63 Found C 57.79, H 6.11, N 9.52

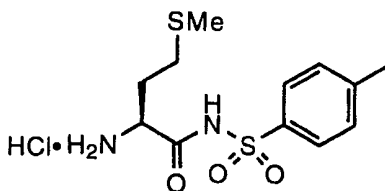
Example 1216

N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine p-tolylsulfonamide hydrochloride salt

Example 1216AN-(tert-Butoxycarbonyl)-methionine p-toluenesulfonamide

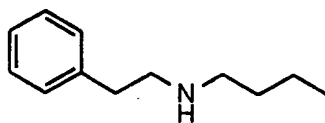
14970 N-(tert-Butoxycarbonyl)-methionine (960 mg, 3.85 mmol) was dissolved in  $\text{CH}_2\text{Cl}_2$  (50 mL), then added EDCI•HCl (1.12 g, 5.85 mmol), DMAP (287 mg, 2.35 mmol), and p-toluenesulfonamide (1.71 g, 10.0 mmol). The reaction was stirred at RT overnight, concentrated, dissolved in EtOAc (130 mL), then washed with water, 2N HCl, water, and brine. After drying over  $\text{Na}_2\text{SO}_4$ , filtration, and concentration, the compound

14975 was purified by chromatography using 1/1 hex/ EtOAc, then EtOAc. Recovered 635 mg (41%). MS (APCI) 403 ( $\text{M}+\text{H}$ )<sup>+</sup>.

Example 1216BMethionine p-toluenesulfonamide hydrochloride salt

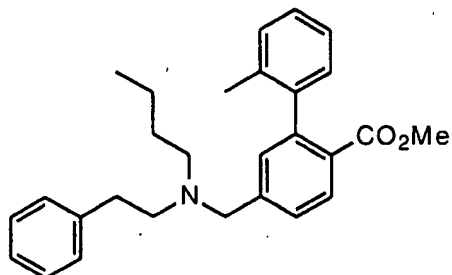
14980 The compound described in Example 1216A (610 mg, 1.52 mmol) was dissolved in 4N HCl in dioxane (10 mL), stirred at RT for 45 min., then diluted with  $\text{Et}_2\text{O}$ . The resultant solids were filtered off, and washed with  $\text{Et}_2\text{O}$  to give 465 mg (90%) white solids. MS ( $\text{DCI}/\text{NH}_3$ ) 303 ( $\text{M}+\text{H}$ )<sup>+</sup>.

14985

Example 1216CN-Butyl-2-phenylethylamine

14990 2-Phenethylamine (12.5 mL, 12.1 g, 99.5 mmol), butyraldehyde (13.2 mL, 10.8 g, 150 mmol), and 3Å molecular sieves were stirred at 50 °C for 1 h, then at RT for 5.5 h. The reaction was then diluted with  $\text{CH}_2\text{Cl}_2$ , filtered through celite, then concentrated to an oil. That oil was dissolved in absolute EtOH (150 mL-previously cooled to 0 °C), and  $\text{NaBH}_4$  (5.7 g, 150 mmol) was added. The reaction was stirred at RT overnight, concentrated, partitioned between water and  $\text{Et}_2\text{O}$ , then the organic layer was washed with

14995 water and brine. After drying over  $\text{Na}_2\text{SO}_4$ , filtration, and concentration, the compound was purified by vacuum distillation using a 6" Vigreux column (98-100 °C/ 9 mm). Recovered 8.2 g (46%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.30 (m, 2H), 7.20 (m, 3H), 2.84 (m, 4H), 2.61 (dd, 2H), 1.43 (m, 2H), 1.32 (m, 2H), 1.08 (br s, 1H), 0.88 (t, 3H).

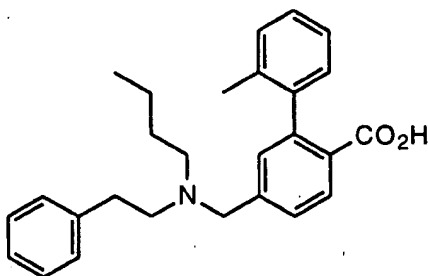


15000

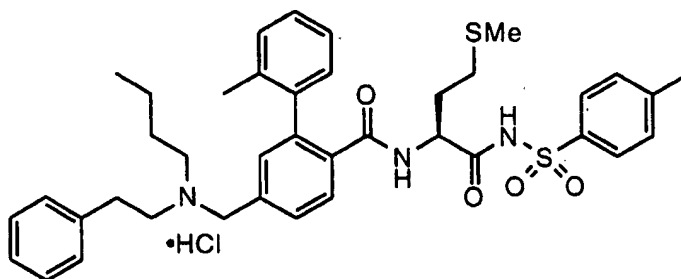
Example 1216D4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

The title compound was prepared from the compound described in Example 1216C and the bromide described in Example 1178D using the method of Example 1178G. MS

15005 (APCI) 416 ( $\text{M}+\text{H}$ ) $^+$ .

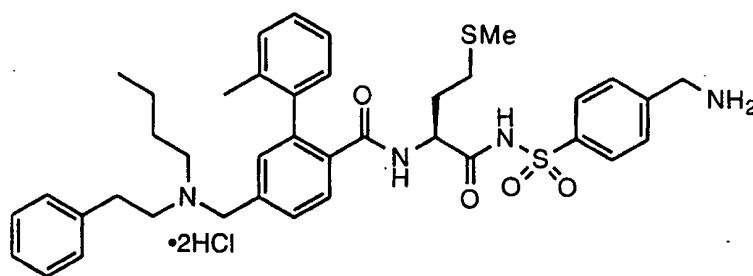
Example 1216E4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

15010 The title compound was prepared from the compound described in Example 1216D using the method of Example 1178H. MS (ESI) 402 ( $\text{M}+\text{H}$ ) $^+$ .

Example 1216F

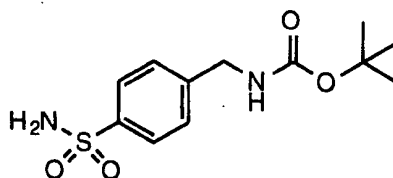
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine p-tolylsulfonimide hydrochloride salt

The above compound was prepared according to the method of Example 1205D using the compounds described in Examples 1216B and 1216E, except the order of the aqueous work-up was saturated NaHCO<sub>3</sub>, 2N HCl, brine, and the chromatography used 98/2/0.5 CHCl<sub>3</sub>/MeOH/CH<sub>3</sub>CO<sub>2</sub>H. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.85 (m, 4H), 7.26 (m, 12H), 6.47 (m, 1H), 4.60 (m, 1H), 4.30 (m, 2H), 3.20 (m, 6H), 2.43 (s, 3H), 2.08 (m, 3H), 1.90 (m, 7H), 1.83, 1.60 (both m, total 4H), 0.95 (m, 3H). MS (ESI) 684 (M-H)<sup>-</sup>. Anal calcd for C<sub>39</sub>H<sub>48</sub>ClN<sub>3</sub>O<sub>4</sub>S<sub>2</sub>: C, 64.84; H, 6.70; N, 5.82; Cl, 4.91. Found: C, 64.62; H, 6.82; N, 5.69; Cl, 4.62.



Example 1217

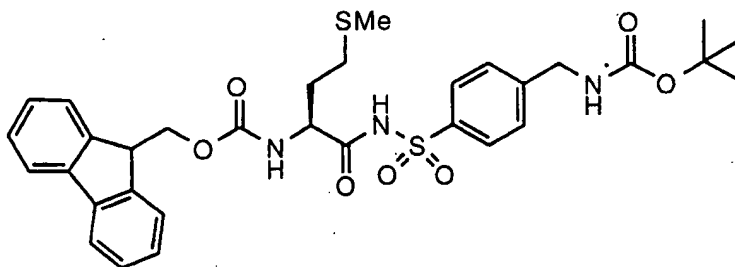
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine 4-(aminomethyl)phenylsulfonimide dihydrochloride salt



Example 1217A

4-[(tert-Butoxycarbonyl)aminomethyl]phenylsulfonamide

4-(Aminomethyl)phenylsulfonamide hydrochloride salt hemihydrate (1.0 g, 4.3 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (20 mL), then triethylamine (0.66 mL, 0.48 g, 4.8 mmol) and di-tert-butyl-dicarbonate (0.95 g, 4.3 mmol) were added. The reaction was stirred at RT overnight, then concentrated and partitioned between water and EtOAc. The organic layer was washed with 2N HCl, saturated aqueous NaHCO<sub>3</sub> and brine, then dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and concentration recovered 1.3 g tacky white solids. MS (DCI/NH<sub>3</sub>) 304 (M+H+NH<sub>3</sub>)<sup>+</sup>.

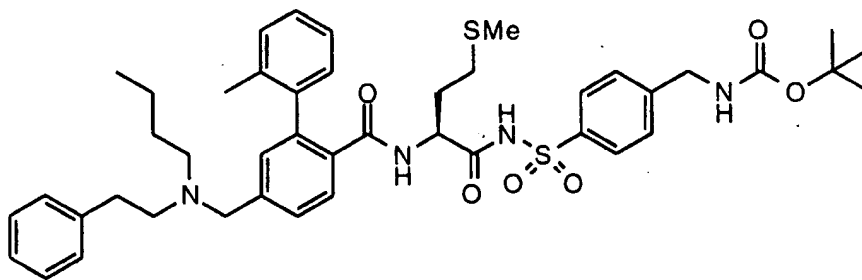
Example 1217B

15045

N-(9-Fluorenylmethoxycarbonyl)-methionine 4-[(tert-butoxycarbonyl)aminomethyl]phenylsulfonimide

Using N-(9-Fluorenylmethoxycarbonyl)-methionine and the compound described in Example 1217A, the title compound was prepared by the method of Example 1216A. MS (ESI) 638 (M-H)<sup>-</sup>.

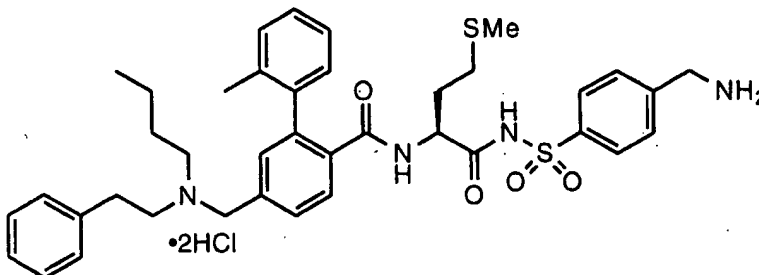
15050

Example 1217C

N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine 4-[(tert-butoxycarbonyl)aminomethyl]phenylsulfonimide

15055

The compound described in Example 1217B was treated with piperidine in CH<sub>2</sub>Cl<sub>2</sub> to give the free amine which was not purified, but directly reacted with the compound described in Example 1216E by the method of Example 1216F to give the title compound. MS (ESI) 801 (M+H)<sup>+</sup>.

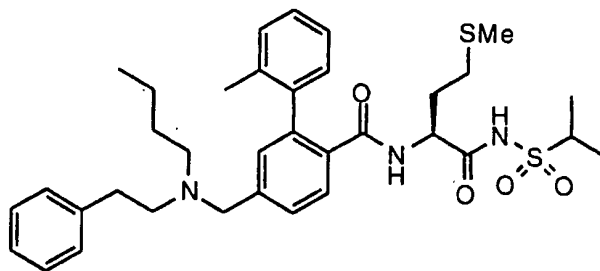


15060

Example 1217D

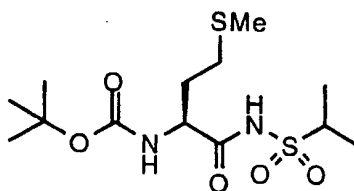
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine 4-(aminomethyl)phenylsulfonimide dihydrochloride salt

Starting with the compound described in Example 1217C, the title compound was prepared by the method of Example 1216B. <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 8.05 (d, 2H), 7.66 (m, 4H), 7.45 (br s, 1H), 7.25 (m, 10H), 4.53 (d, 2H), 4.25 (m, 1H), 4.24 (s, 2H), 3.33 (m, 2H), 3.24 (m, 2H), 3.10 (m, 2H), 2.10 (m, 5H), 1.97 (s, 3H), 1.80 (m, 3H), 1.60 (m, 1H), 1.40 (m, 2H), 0.98 (t, 3H). MS (ESI) 699 (M-H)<sup>-</sup>. Anal calcd for C<sub>39</sub>H<sub>50</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>4</sub>S<sub>2</sub> · 1.50 H<sub>2</sub>O : C, 68.49; H, 6.67; N, 7.00. Found: C, 58.41; H, 6.61; N, 6.70.



#### Example 1218

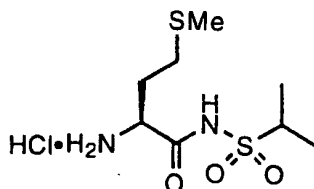
N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine isopropylsulfonimide



#### Example 1218A

N-(tert-Butoxycarbonyl)-methionine isopropylsulfonimide

The title compound was prepared by the method of Example 1216A using isopropylsulfomamide. MS (DCI/NH<sub>3</sub>) 372 (M+H+NH<sub>3</sub>)<sup>+</sup>.



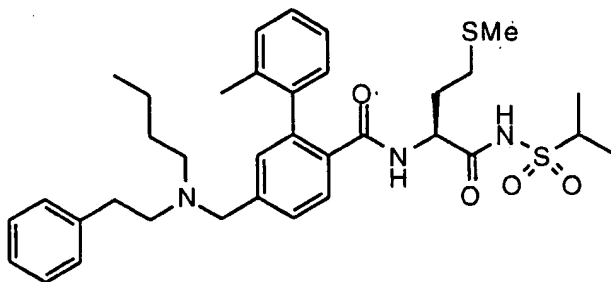
#### Example 1218B

Methionine isopropylsulfonimide hydrochloride salt



Starting with the compound described in Example 1218A, the title compound was prepared by the method of Example 1216B, except the product was isolated as a tan foam after stripping off the dioxane. MS (DCI/NH<sub>3</sub>) 255 (M+H)<sup>+</sup>.

15090



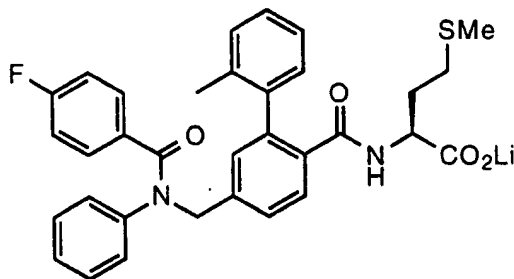
### Example 1218C

#### N-[4-(N-Butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine isopropylsulfonimide

15095

The above compound was prepared according to the method of Example 1205D using the compounds described in Examples 1218B and 1216E, except the order of the aqueous work-up was saturated NaHCO<sub>3</sub>, 2N HCl, brine, and the chromatography used 98/2/0.5 CHCl<sub>3</sub>/MeOH/CH<sub>3</sub>CO<sub>2</sub>H. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.91 (m, 1H), 7.43 (d, 1H), 7.32 (m, 3H), 7.18 (m, 7H), 5.83 (d, 1H), 4.43 (m, 1H), 3.77 (s, 2H), 3.65 (m, 1H), 2.80 (br s, 4H), 2.59 (m, 2H), 2.15, 2.02 (both m, total 8H), 1.82 (m, 1H), 1.50, 1.38, 1.28 (all m, total 11H), 0.86 (t, 3H). MS (ESI) 636 (M-H)<sup>-</sup>. Anal calcd for C<sub>35</sub>H<sub>47</sub>N<sub>3</sub>O<sub>4</sub>S<sub>2</sub>: C, 65.90; H, 7.43; N, 6.59. Found: C, 66.01; H, 7.36; N, 6.30.

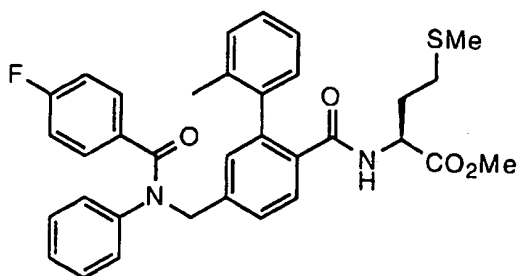
15100



15105

### Example 1227

#### N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

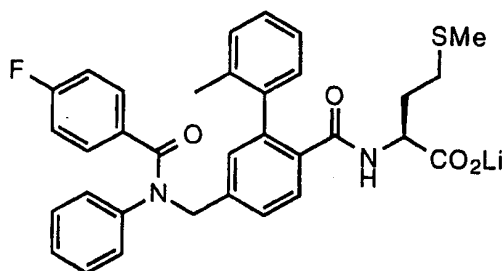


15110

Example 1227AN-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15115 A mixture of 4-fluorobenzoyl chloride (0.053 g, 0.33 mmol), 1236C (0.103 g, 0.22 mmol), and 0.2 ml of pyridine in 5 ml of  $\text{CH}_2\text{Cl}_2$  was stirred for 12 hours. The mixture was washed with 10% HCl and brine respectively, dried over  $\text{MgSO}_4$ . Flash chromatography of the residue eluting with 1:1 EtOAc/Hexane afforded 0.13 g of the title compound (99%).

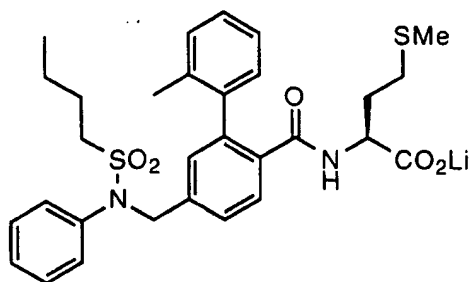
15120 NMR( $\text{CDCl}_3$ ) 7.84-7.94 (m, 1H); 7.38-7.48 (m, 1H); 7.05-7.38 (m, 10H); 5.85-5.92 (m, 1H); 5.10-5.27 (m, 2H); 4.56-4.67 (m, 1H); 3.62 (s, 3H); 1.95-2.20 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/ $\text{NH}_3$ )/MS: 585( $\text{M}+\text{H}$ )<sup>+</sup>; 604 ( $\text{M}+\text{NH}_4$ )<sup>+</sup>.

Example 1227BN-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

15125

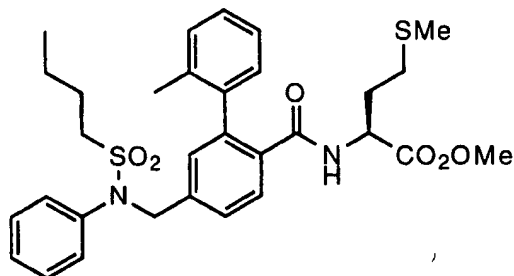
Prepared according to the procedure of example 1178J from 1227A. NMR  $^1\text{H}$ ( $\text{MeOH}-d_4$ ): 7.6-7.7 (1H, m); 7.3-7.5 (3H, m); 6.9-7.3 (14H, m); 5.18-5.38 (2H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 569( $\text{M}-\text{Li}$ ).

15130

Example 1228

N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

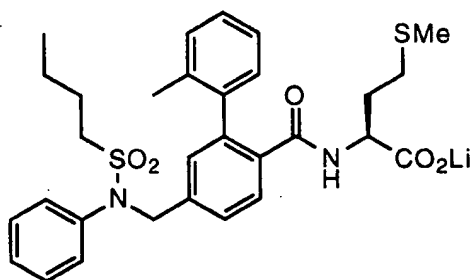
15135

Example 1228A

N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15140

Prepared to the procedure of example 1229A from the reaction between 1236C and butanesulfonyl chloride. NMR(CDCl<sub>3</sub>) 7.80-7.90 (m, 1H); 7.12-7.38 (m, 10H); 7.05-7.11 (m, 1H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 3.0-3.08 (m, 2H); 1.5-2.15 (m, 14H); 0.92-0.98 (m, 3H). (ESI/NH<sub>3</sub>)/MS: 583(M+H)<sup>+</sup>; 600(M+NH<sub>4</sub>)<sup>+</sup>.



15145

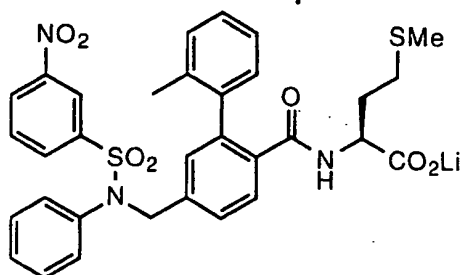
Example 1228B

N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1228A. NMR

15150

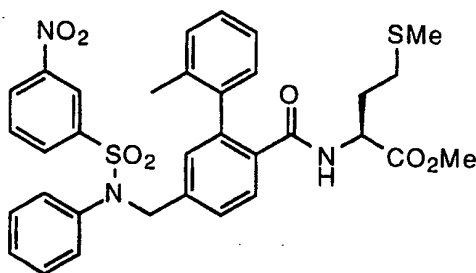
<sup>1</sup>H(MeOH-d<sub>4</sub>): 7.5-7.62 (1H, m); 7.1-7.4 (12H, m); 4.95 (2H, s); 4.1-4.22 (1H, m); 3.1-3.2 (2H, t); 1.7-2.1 (12H, m); 1.4-1.5 (2H, m); 0.9-1.0 (3H, t). ESI(-)/MS: 567(M-Li).



15155

Example 1229

N-[4-N-(N-phenyl)-N-(3-nitrobenzenesulfonyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt



15160

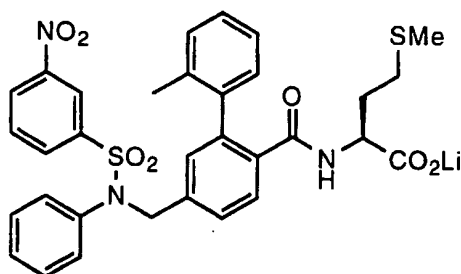
Example 1229A

N-[4-N-(N-phenyl)-N-(3-nitrobenzenesulfonyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine, methyl ester

A mixture of 3-nitrophenylsulfonyl chloride (0.076 g, 0.34 mmol), 1236C (0.106 g, 0.23 mmol), and 0.2 ml of pyridine in 3 ml of CH<sub>2</sub>Cl<sub>2</sub> was stirred for 12 hours. The mixture was washed with 10% HCl and brine respectively, dried over MgSO<sub>4</sub>. Flash chromatography of the residue eluting with 1:1 EtOAc/Hexane afforded 0.12 g of the title compound (80%). NMR(CDCl<sub>3</sub>) 8.56 (m, 1H); 8.40-8.48 (m, 1H); 7.9-7.95 (m, 1H); 7.8-7.91 (m, 1H); 7.68-7.76 (m, 1H); 7.10-7.35 (m, 8H); 7.05 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.81 (s, 2H); 4.5-4.65 (m, 1H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (ESI/NH<sub>3</sub>)/MS: 648(M+H)<sup>+</sup>; 665(M+NH<sub>4</sub>)<sup>+</sup>.

15165

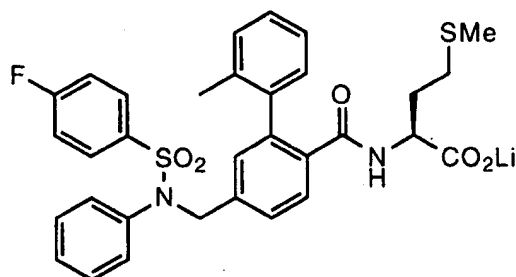
15170



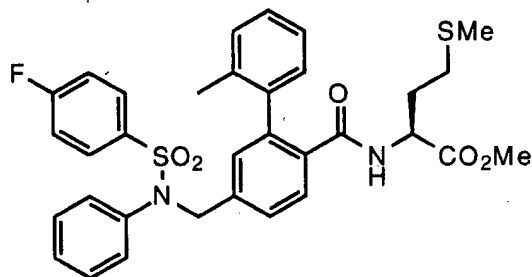
Example 1229B

N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1229A. NMR  $^1\text{H}$ (MeOH- $d_4$ ): 8.35-8.45 (2H, m); 7.78-7.85 (2H, m), 7.5-7.6 (1H, m); 7.3-7.4 (1H, m); 7.1-7.3 (8H, m); 6.95-7.15 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 632(M-Li).

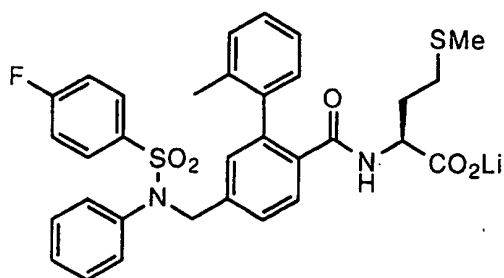
Example 1230

N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1230A

N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1229A from reaction between 1236C and 4-fluorophenylsulfonyl chloride. NMR( $\text{CDCl}_3$ ) 7.78-7.82 (m, 1H); 7.58-7.68 (m, 2H); 7.25-7.32 (m, 10H); 7.08 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.79 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/ $\text{NH}_3$ )/MS: 621(M+ $\text{NH}_4$ ) $^+$ ; 638(M+ $\text{NH}_4$ ) $^+$ .

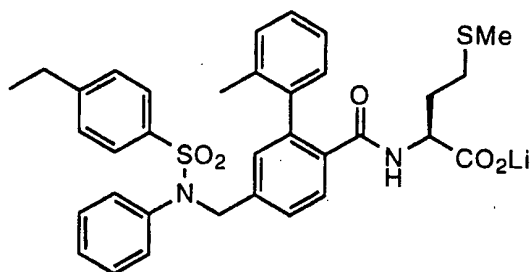
Example 1230B

N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

15200

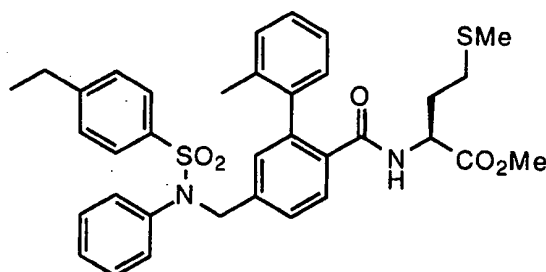
Prepared according to the procedure of example 1178J from 1230A. NMR  $^1\text{H}$ (MeOH- $d_4$ ): 7.65-7.8 (2H, m); 7.5-7.6 (1H, m); 7.1-7.3 (11H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 605(M-Li).

15205

Example 1231

N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

15210

Example 1231A

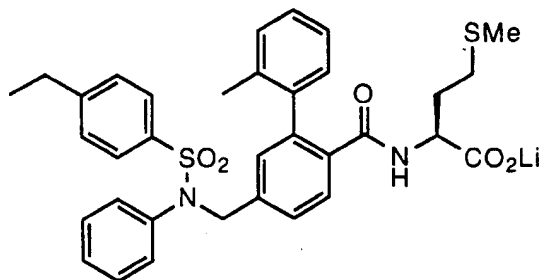
N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15215

Prepared according to the procedure of example 1229A from reaction between 1236C and 4-ethylphenylsulfonyl chloride. NMR( $\text{CDCl}_3$ ) 7.78-7.82 (m, 1H); 7.55-7.60 (m, 2H); 7.25-7.32 (m, 10H); 7.08 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.76 (s,

2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.7-2.78(m, 2H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H); 1.2-1.35(m, 3H). (DSI/NH<sub>3</sub>)/MS: 631(M+H)<sup>+</sup>; 648(M+NH<sub>4</sub>)<sup>+</sup>.

15220

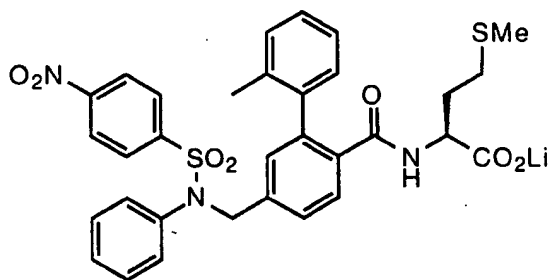
Example 1231

N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

15225

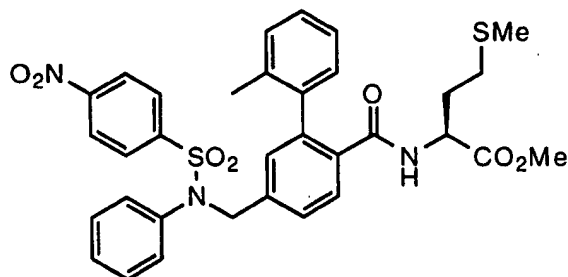
Prepared according to the procedure of example 1178J from 1231A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.5-7.6 (3H, m); 7.1-7.4 (9H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 2.7 (2H, q) 1.7-2.1 (10H, m) (1H, m); 1.25 (3H, t). ESI(-)/MS: 615(M-Li).

15230

Example 1232

N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

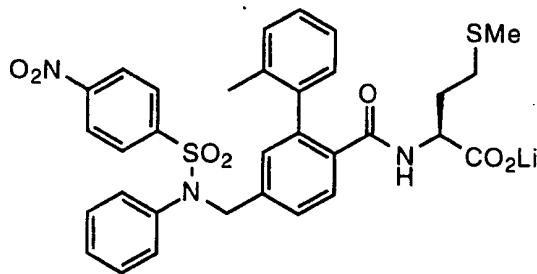
15235

Example 1232A

N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1229A from reaction between  
 15240 1236C and 4-nitrophenylsulfonyl chloride. NMR(CDCl<sub>3</sub>) 8.56 (m, 1H); 8.40-8.48 (m, 1H); 7.9-7.95 (m, 1H); 7.8-7.91 (m, 1H); 7.68-7.76 (m, 1H); 7.10-7.35 (m, 8H); 7.05 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.81 (s, 2H); 4.5-4.65 (m, 1H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 648(M+H)<sup>+</sup>; 665(M+NH<sub>4</sub>)<sup>+</sup>.

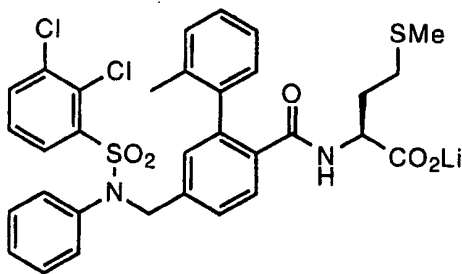
15245

Example 1232B

N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

15250 Prepared according to the procedure of example 1178J from 1232A. NMR  
<sup>1</sup>H(MeOH-d<sub>4</sub>): 8.45-8.55 (1H, m); 8.35-8.38 (1H, m); 8.0-8.1 (1H, m); 7.8-7.9 (1H, m); 7.5-7.7 (1H, m); 7.3-7.4 (1H, m); 7.1-7.3 (8H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 632(M-Li).

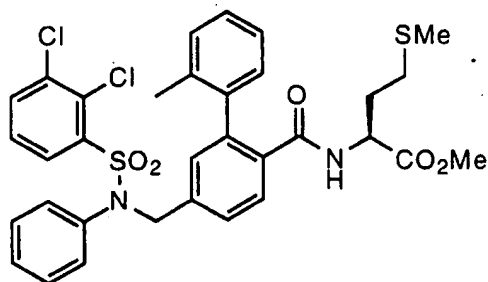
15255

Example 1233

N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

15260

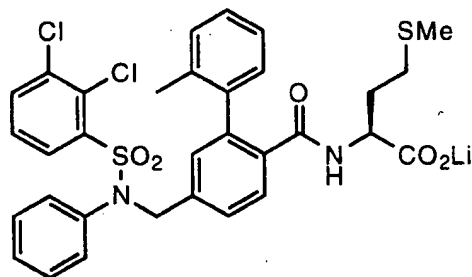


Example 1233A

N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

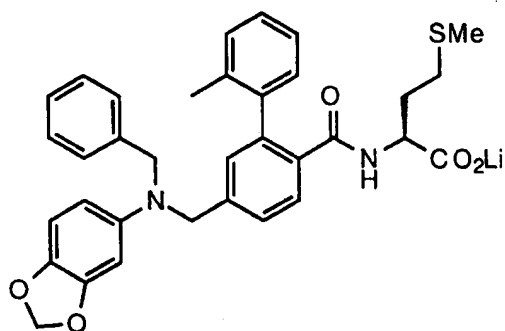
15265 Prepared according to the procedure of example 1229A from reaction between 1236C and 3,4-dichlorophenylsulfonyl chloride. NMR(CDCl<sub>3</sub>) 7.6-7.7 (m, 1H); 7.5-7.55 (m, 1H); 7.55-7.6 (m, 1H); 7.40-7.43 (m, 1H); 7.15-7.36 (m, 8H); 7.08 (m, 1H); 6.95-7.01 (m, 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 671(M+NH<sub>4</sub>)<sup>+</sup>.

15270

Example 1233B

N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

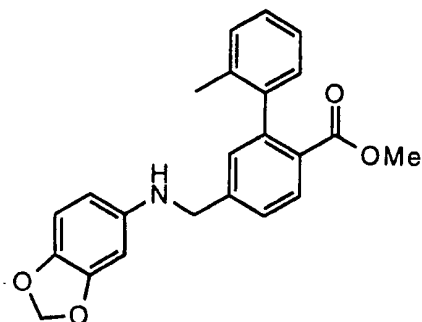
15275 Prepared according to the procedure of example 1178J from 1233A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.7-7.8 (2H, m); 7.5-7.6 (2H, m); 7.1-7.3 (9H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 655(M-Li).



15280

Example 1234

N-[4-N-(N-3,4-(methylenedioxy)phenyl)-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

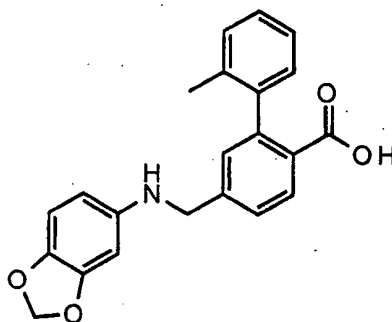


15285

Example 1234A

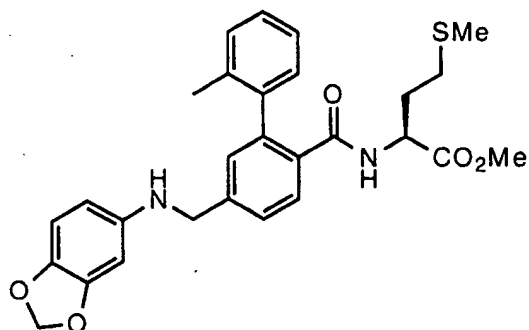
Prepared according to the procedure of example 1236A. Instead of using aniline, 3,4-(methylenedioxy)aniline was used to make the title compound. NMR(CDCl<sub>3</sub>) 7.90-7.96 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.30 (m, 4H); 7.00-7.18 (m, 1H); 6.80-6.83 (m, 1H); 6.22-6.26 (m, 1H); 6.00-6.08 (m, 1H); 5.82 (s, m); 4.32-4.39 (m, 2H); 3.95-4.00 (m, 1H); 3.60 (s, 3H); 2.05 (s, 3H). (ESI/NH<sub>3</sub>)/MS: 376(M+H)<sup>+</sup>; 373(M+NH<sub>4</sub>)<sup>+</sup>.

15290

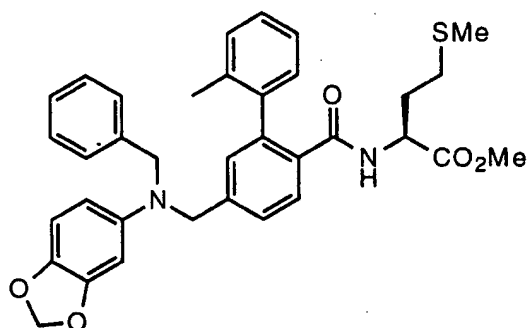
Example 1234B

Prepared according to the procedure of example 1178H from 1234A. NMR(CDCl<sub>3</sub>) 7.90-7.96 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.30 (m, 4H); 7.00-7.18 (m, 1H); 6.80-6.83 (m, 1H); 6.22-6.26 (m, 1H); 6.00-6.08 (m, 1H); 5.82 (s, 2H); 4.32-4.39 (m, 2H); 3.95-4.00 (m, 1H); 2.05 (s, 3H). (ESI/NH<sub>3</sub>)/MS: 362(M+H)<sup>+</sup>; 351(M+NH<sub>4</sub>)<sup>+</sup>.

15295

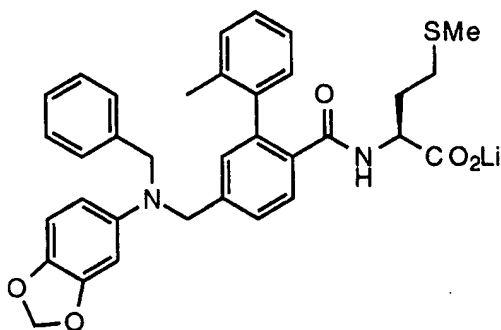
Example 1234C

Prepared according to the procedure of example 1178I from 1234B. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.18-7.30 (m, 6H); 7.00-7.18 (m, 1H); 6.6-6.65 (m, 1H); 6.35-6.40 (m, 1H); 6.10-6.20 (m, 1H); 5.82 (m, 3H); 4.5-4.70 (m, 3H); 3.61 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 507(M+H)<sup>+</sup>; 324(M+NH<sub>4</sub>)<sup>+</sup>.

Example 1234D

N-[4-N-(N-(3,4-methylenedioxy)phenyl)-N-(4-fluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine, methyl ester

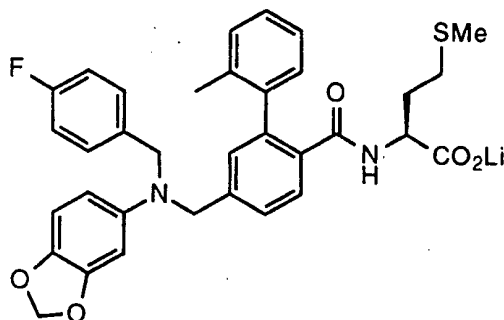
Prepared according to the procedure of example 1236A from reaction between 1235C and benzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.18-7.30 (m, 10H); 7.02-7.18 (m, 1H); 6.6-6.65 (m, 1H); 6.35-6.40 (m, 1H); 6.15-6.20 (m, 1H); 5.82 (m, 3H); 4.59-4.70 (m, 3H); 4.57 (s, 2H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 597(M+H)<sup>+</sup>.



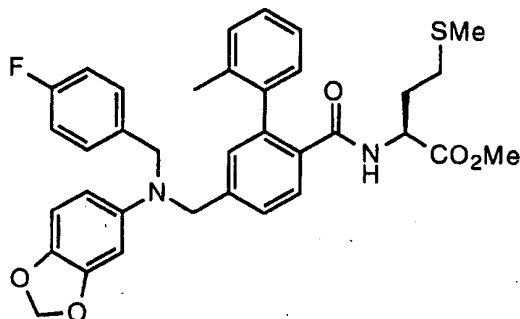
Example 1234E

N-[4-N-(N-3,4-(methylenedioxy)phenyl)-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1234D. NMR  $^1\text{H}$ (MeOH- $d_4$ ): 7.5-7.6 (1H, m); 7.2-7.25 (1H, m); 7.0-7.2 (9H, m); 6.9-7.0 (2H, m); 6.5-6.57 (1H, m); 6.3 (1H, m); 6.1 (1H, m); 5.75 (2H, s); 4.45 (2H, s); 4.4 (2H, s); 4.1-4.2 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 581(M-Li).

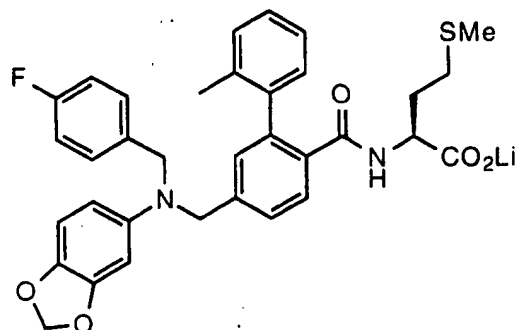
Example 1235

N-[4-N-(N-3,4-(methylenedioxy)phenyl)-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1235A

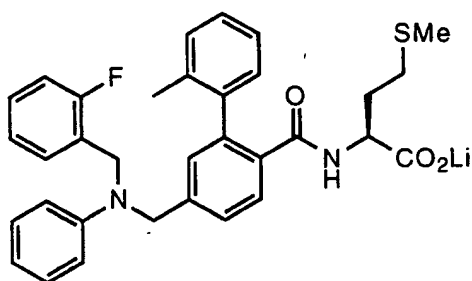
N-[4-N-(N-3,4-(methylenedioxy)phenyl)-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1234C and 4-fluorobenzyl bromide. NMR( $\text{CDCl}_3$ ) 7.85-7.95 (m, 1H); 7.18-7.61 (m, 7H); 6.92-7.18 (m, 3H); 6.6-6.65 (m, 1H); 6.35-6.40 (m, 1H); 6.15-6.20 (m, 1H); 5.82 (m, 3H); 4.57-4.65 (m, 1H); 4.53 (s, 2H); 4.50 (s, 2H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (ESI/ $\text{NH}_3$ )/MS: 614(M+H) $^+$ .

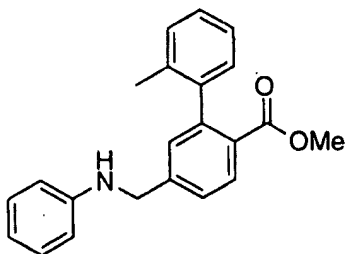
Example 1235B

N-[4-N-(N-3,4-(methylenedioxy)phenyl)-N-(4-fluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1235A. NMR  $^1\text{H}(\text{MeOH}-d_4)$ : 7.5-7.6 (1H, m); 7.2-7.25 (1H, m); 7.0-7.2 (8H, m); 6.9-7.0 (2H, m); 6.5-6.57 (1H, m); 6.3 (1H, m); 6.1 (1H, m); 5.75 (2H, s); 4.45 (2H, s); 4.4 (2H, s); 4.1-4.2 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 599(M-Li).

Example 1236

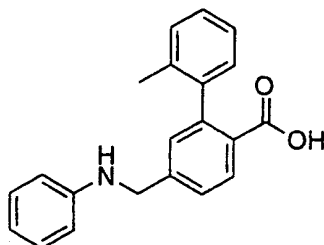
N-[4-N-(N-phenyl)-N-(2-fluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1236A

4-(N-phenyl)aminomethyl-2-(2-methylphenyl)benzoic acid, methyl ester

A mixture of 4-Bromomethyl-2-(2-methylphenyl)benzoic acid, methyl ester (6.12 g, 20 mmol), aniline (1.68 g, 20 mmol),  $\text{NaHCO}_3$  (1.68 g, 40 mmol), and  $\text{Bu}_4\text{N}^+\text{I}^-$  (0.74g, 2

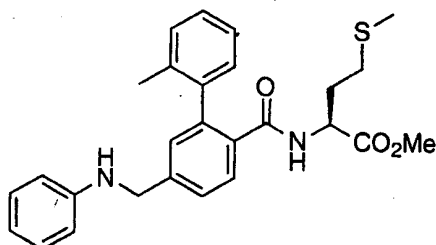
mmol) in 50 ml of DMF was heated at 75°C under N<sub>2</sub> for 12 hours. The reaction mixture was quenched by adding 400 ml of water. The solution was then extracted by 300 ml of EtOAc, washed by brine and dried over MgSO<sub>4</sub>. Flash chromatography of residue on silica gel eluting with 80:20 EtOAc/Hexane afforded 6.1 g of pure product(96%). NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.40-7.45 (m, 1H); 7.0-7.36 (m, 7H); 6.68-6.78 (m, 1H); 6.58-6.65 (m, 2H); 4.2 (s, 2H); 4.05-4.2 (m, 1H); 3.58 (s, 3H); 2.05 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 332(M+H)<sup>+</sup>, 349(M+NH<sub>4</sub>)<sup>+</sup>.



#### Example 1236B

##### 4-(N-phenylaminomethyl)-2-(2-methylphenyl)benzoic acid

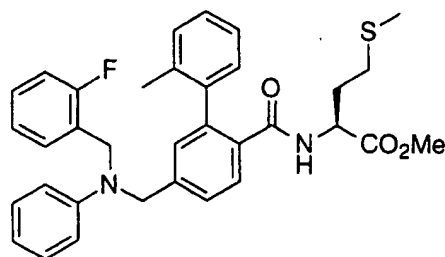
Prepared according to the procedure of example 1178H from 1236A. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.40-7.45 (m, 1H); 7.0-7.36 (m, 7H); 6.68-6.78 (m, 1H); 6.58-6.65 (m, 2H); 4.2 (s, 2H); 4.05-4.2 (m, 1H); 2.05 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 318(M+H)<sup>+</sup>, 335(M+NH<sub>4</sub>)<sup>+</sup>.



#### Example 1236C

##### N-4-[(N-phenylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

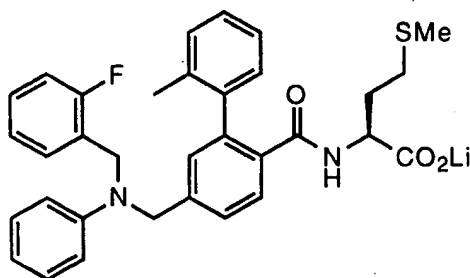
Prepared according to the procedure of example 1178I from 1236B. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.41-7.47 (m, 1H); 7.1-7.36 (m, 7H); 6.68-6.78 (m, 1H); 6.58-6.65 (m, 2H); 5.85-5.95 (m, 1H); 4.56-4.68 (m, 1H); 4.2 (s, 2H); 4.05-4.2 (m, 1H); 3.62 (s, 3H); 2.05 (s, 3H); 2.0-2.15 (m, 8H), 1.7-2.0 (m, 1H), 1.5-1.7 (m, 1H).. (DSI/NH<sub>3</sub>)/MS: 463(M+H)<sup>+</sup>, 480(M+NH<sub>4</sub>)<sup>+</sup>.

Example 1236DN-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15390

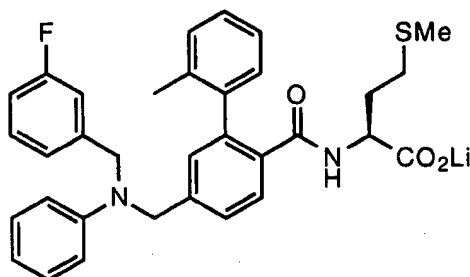
Prepared according to the procedure of 1236A from reaction between 1236C and 2-fluorobenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.0-7.4 (m, 12H); 6.65-6.78 (m, 3H); 5.8-5.9 (m, 1H); 4.75 (m, 4H); 4.58-4.65 (m, 1H); 3.65 (s, 3H), 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). MS/(DSI/NH<sub>3</sub>): 571(M+H)<sup>+</sup>.

15395

Example 1236EN-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

15400

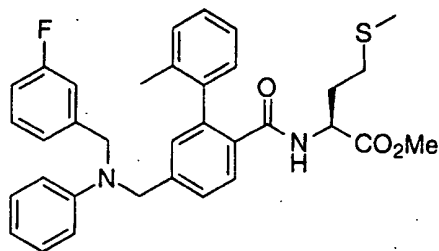
Prepared according to the procedure of example 1178J for making lithium salt. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, d); 7.3-7.4 (1H, d); 7.0-7.4 (9H, m); 6.6-6.85 (6H, m); 4.7 (2H, s); 4.65 (2H, s); 4.2-4.3 (1H, m); 1.5-2.2 (10H, m). ESI(-)/MS: 555(M-Li).



15405

Example 1237

N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



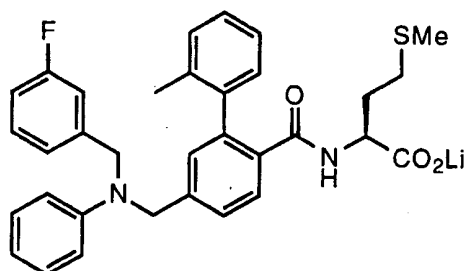
15410

Example 1237A

N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of 1236A from reaction between 1236C and 3-fluorobenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 6.9-7.4 (m, 12H); 6.75-6.8 (m, 3H); 5.8-5.9 (m, 1H); 4.70 (s, 2H); 4.58-4.65 (m, 3H); 3.62 (s, 3H); 2.0-2.15 (m, 8H), 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (ESI/NH<sub>3</sub>)/MS: 571(M+H)<sup>+</sup>.

15415



15420

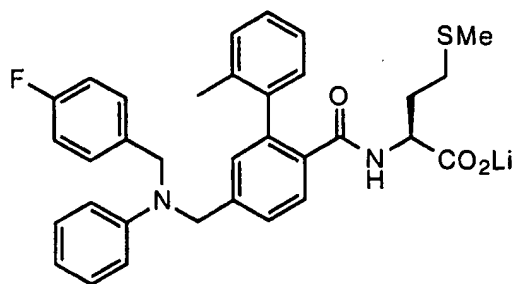
Example 1237B

N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1237A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (2H, m); 6.86-7.4 (10H, m); 6.6-6.85 (4H, m); 4.75-4.85 (4H, m); 4.18-4.3 (1H, m); 1.6-2.2 (10H, m). ESI(-)/MS: 555(M-Li).

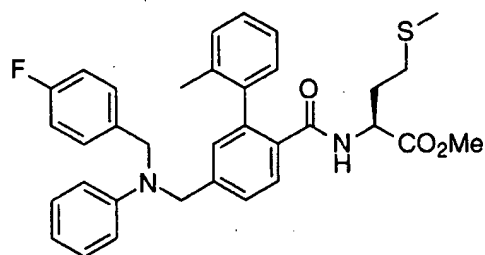
15425



Example 1238

15430

N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

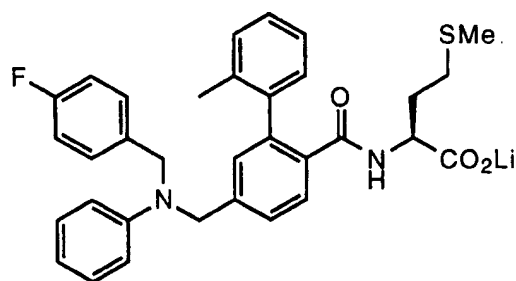
Example 1238A

15435

N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of 1236A from reaction between 1236C and 4-fluorobenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.15-7.4 (m, 9H); 6.95-7.15 (m, 3H); 6.7-6.8 (m, 3H); 5.8-5.9 (m, 1H); 4.70 (s, 2H); 4.58-4.65 (m, 3H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 571(M+H)<sup>+</sup>.

15440

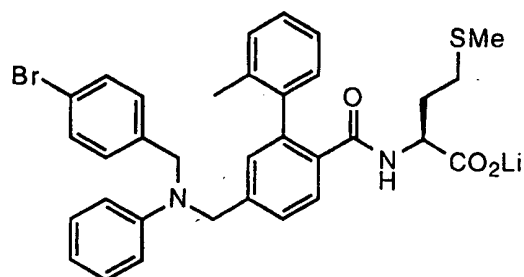
Example 1238B

15445

N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

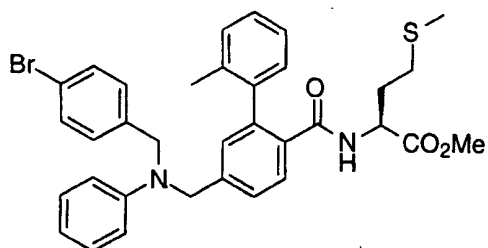
Prepared according to the procedure of example 1178J from 1238A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (2H, m); 6.86-7.4 (10H, m); 6.6-6.85 (4H, m); 4.65-4.85 (4H, m); 4.18-4.3 (1H, m); 1.6-2.2 (10H, m). ESI(-)/MS: 555(M-Li).

15450

Example 1239

N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

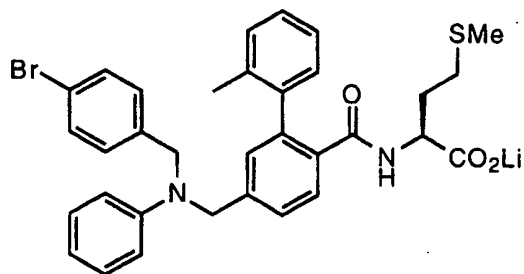
15455

Example 1239A

N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15460

Prepared according to the procedure of example 1236A from reaction between 1236C and 4-bromobenzyl bromide. NMR(CDCI<sub>3</sub>) 7.85-7.95 (m, 1H); 7.05-7.48 (m, 12H); 6.65-6.78 (m, 3H); 5.8-5.9 (m, 1H); 4.75 (s, 2H); 4.55-4.65 (m, 3H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (ESI/NH<sub>3</sub>)/MS: 631(M+H)<sup>+</sup>.



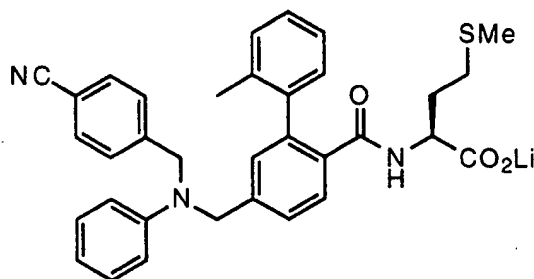
15465

Example 1239B

N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1239A. NMR

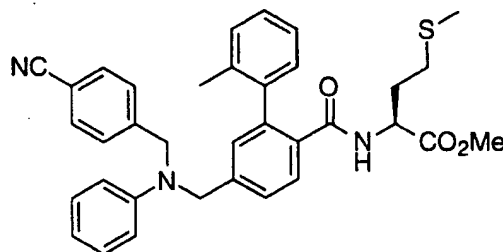
15470  $^1\text{H}$ (MeOH- $d_4$ ): 7.58-7.67 (1H, d); 7.38-7.46 (2H, d); 7.3-7.39 (H, d); 7.0-7.3 (11H, m); 6.6-6.8 (3H, m); 4.75 (2H, s); 4.65 (2H, s); 4.18-4.3 (1H, m); 1.5-2.2 (10H, m). ESI(-)/MS: 615(M-Li), 573.



15475

Example 1240

N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



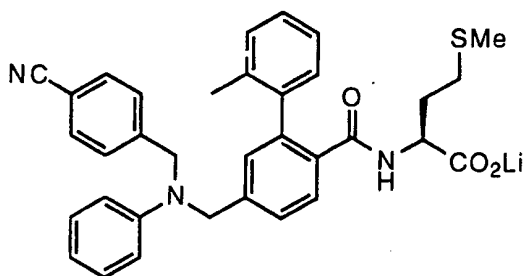
15480

Example 1240A

N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between

15485 1236C and 4-cyanobenzyl bromide. NMR( $\text{CDCl}_3$ ) 7.85-7.95 (m, 1H); 7.58-7.65 (m, 2H); 7.1-7.4 (m, 10H); 6.65-6.80 (m, 3H); 5.8-5.9 (m, 1H); 4.65 (m, 4H); 4.58-4.64 (m, 1H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/ $\text{NH}_3$ )/MS: 578(M+H) $^+$ .

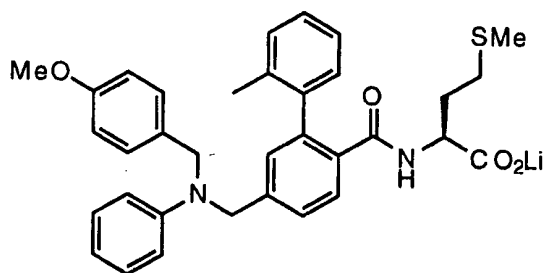


15490

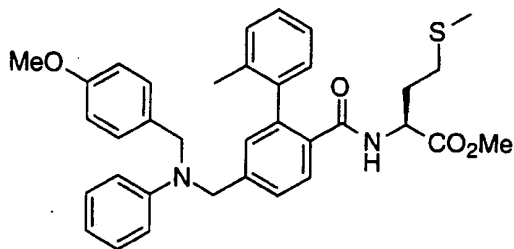
Example 1240BN-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1240A. NMR

15495  $^1\text{H}$ (MeOH- $d_4$ ): 7.6-7.7 (3H, m); 7.4-7.5 (2H, m); 7.35-7.4 (1H, m); 7.02-7.3 (10H, m); 6.6-6.7 (3H, m) 4.9 (2H, s); 4.75 (2H, s); 4.18-4.3 (1H, m); 1.5-2.2 (10H, m). ESI(-)/MS: 562(M-Li).



15500

Example 1241N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

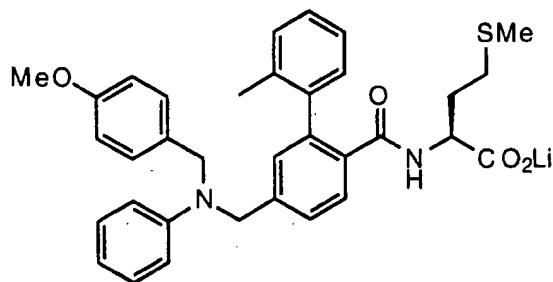
15505

Example 1241AN-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between

15510 1236C and 4-methoxybenzyl bromide. NMR( $\text{CDCl}_3$ ) 7.85-7.95 (m, 1H); 7.15-7.4 (m,

12H); 6.8-6.9 (m, 1H); 6.7-6.8 (m, 2H); 5.8-5.9 (m, 1H); 4.65 (m, 3H); 4.60 (s, 2H); 3.81 (s, m); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (ESI/NH<sub>3</sub>)/MS: 583(M+H)<sup>+</sup>.



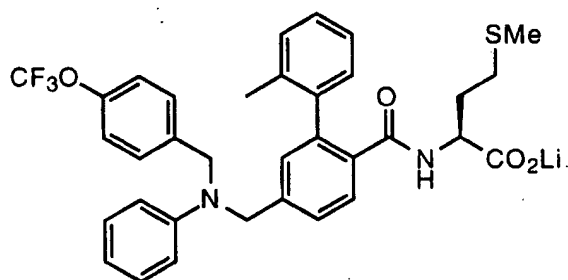
15515

Example 1241B

N-[4-N-(N-phenyl)-N-(4-methoxybenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1241A. NMR

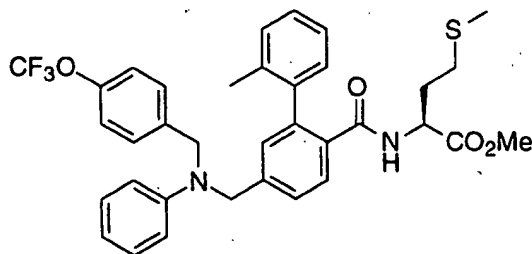
15520 <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.0-7.3 (10H, m); 6.6-6.85 (6H, m); 4.68 (2H, s); 4.58 (2H, s); 4.18-4.3 (1H, m); 3.88 (3H, s); 1.5-2.2 (10H, m). ESI(-)/MS: 567(M-Li); 445.



15525

Example 1242

N-[4-N-(N-phenyl)-N-(4-trifluoromethoxybenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt

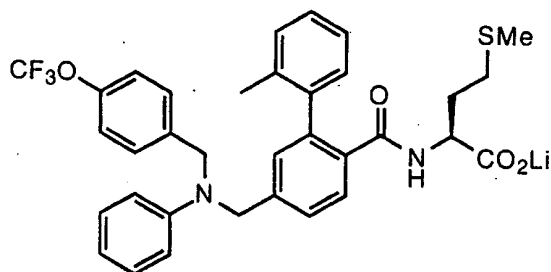


15530

Example 1242A

N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

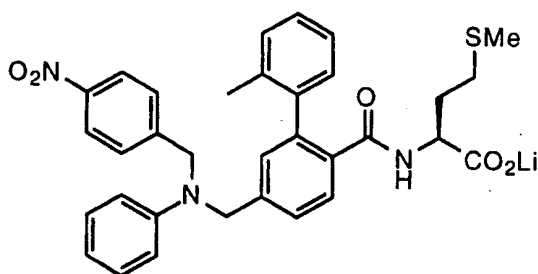
Prepared according to the procedure of example 1236A from reaction between 1236C and 4-trifluoromethoxybenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.15-7.4 (m, 12H); 6.8-6.9 (m, 1H); 6.7-6.8 (m, 2H); 5.8-5.9 (m, 1H); 4.65 (m, 3H); 4.60 (s, 2H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 636(M+H)<sup>+</sup>.



Example 1242B

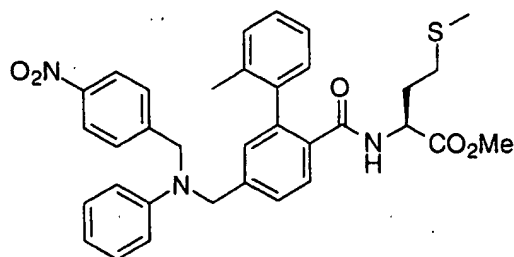
N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1242A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.3-7.4 (3H, d), 7.05-7.25 (9H, m); 6.7-6.8 (2H, m); 6.6-6.7 (1H, m); 4.7-4.8 (4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 621(M-Li).



Example 1243

N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



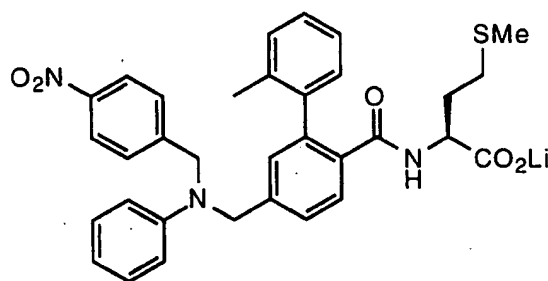
15555

Example 1243A

N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 4-nitrobenzyl bromide. NMR(CDCl<sub>3</sub>) 8.15-8.20 (m, 2H); 7.85-7.95 (m, 1H); 7.1-7.45 (m, 10H); 6.75-6.81 (m, 1H); 6.65-6.71 (m, 2H); 5.78-5.88 (m, 1H); 4.7-4.8 (ss, 4H); 4.6-4.75 (m, 1H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 598(M+H)<sup>+</sup>; 615 (M+NH<sub>4</sub>)<sup>+</sup>.

15560



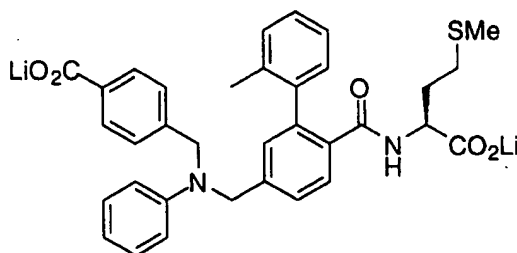
15565

Example 1243B

N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1243A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 8.15-8.2 (2H, m); 7.6-7.7 (1H, m), 7.48-7.56 (2H, m); 7.35-7.41 (1H, m); 7.15-7.3 (8H, m); 6.65-6.78 (3H, m), 4.78-4.85(4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 582(M-Li).

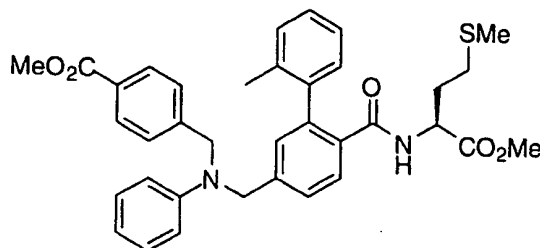
15570



15575

Example 1244

N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt



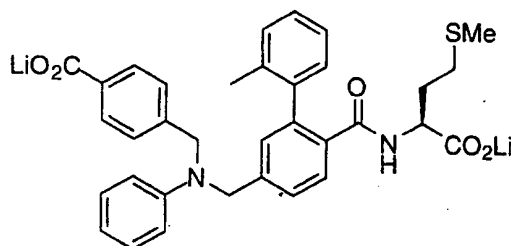
15580

Example 1244A

N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dimethyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and methyl 4-(bromomethyl) benzoate. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.18-7.40 (m, 12H); 6.7-6.85 (m, 3H); 5.8-5.9 (m, 1H); 4.7 (s, 4H); 4.58-4.68 (m, 1H); 3.90 (s, 3H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 628(M+NH<sub>4</sub>)<sup>+</sup>.

15585



15590

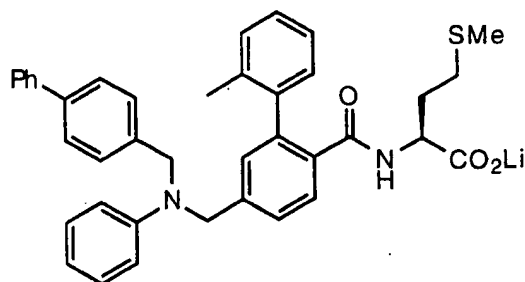
Example 1244B

N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt

Prepared according to the procedure of example 1178J from 1244A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.9-8.0 (2H, m); 7.6-7.7 (1H, m), 7.3-7.4 (2H, m); 7.1-7.28 (9H, m); 6.7-6.75 (2H, m); 6.6-6.7 (1H, m); 4.78 (2H, s); 4.70 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 595(M-Li).

15595

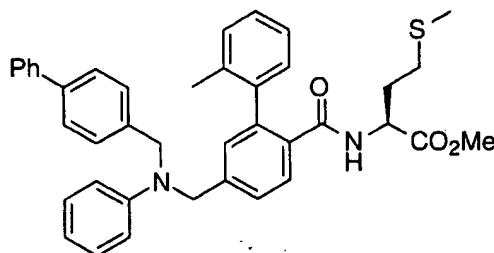




15600

Example 1245

N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



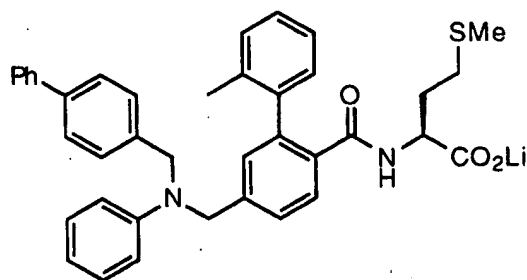
15605

Example 1245 A

N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 4-phenylbenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.1-7.45 (m, 17H); 6.75-6.81 (m, 1H); 6.65-6.7 (m, 3H); 5.8-5.9 (m, 1H); 4.7-4.8 (ss, 4H); 4.6-4.75 (m, 1H); 3.65 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 629(M+H)<sup>+</sup>.

15610

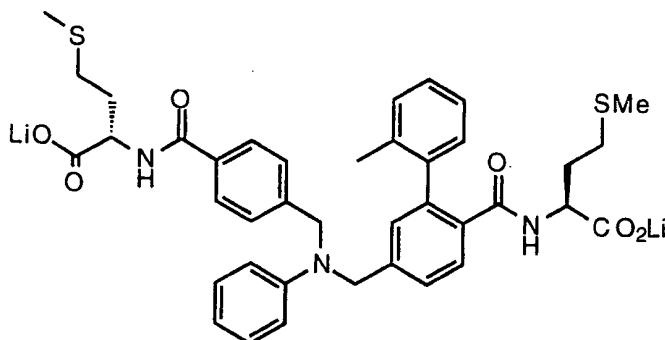


15615

Example 1245B

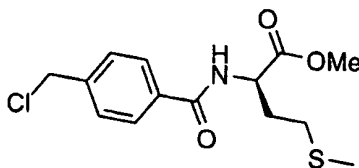
N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1245A. NMR  
 $^1\text{H}$ (MeOH- $d_4$ ): 7.1-7.7 (19H, m); 6.7-6.8 (2H, m); 6.6-6.7 (1H, m); 4.7-4.8 (4H, m);  
 15620 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 613(M-Li).



#### Example 1246

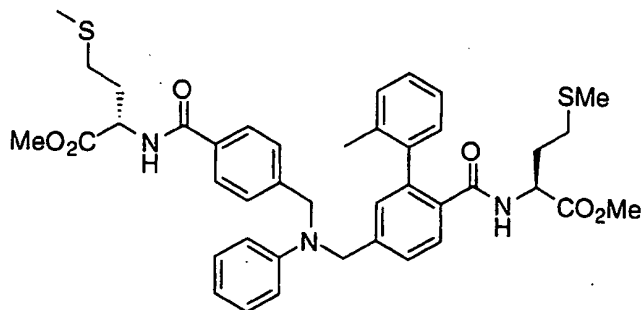
15625 N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.



#### Example 1246A

15630 4-(chloromethyl)-benzoylmethionine, methyl ester

A mixture of 4-(chloromethyl)-benzoyl chloride (0.189 g, 1 mmol), methionine methyl ester hydrochloride (0.199 g, 1 mmol), and 0.5 ml of pyridine in 5 ml of chloroform was stirred for 12 hours. The organic solution was washed with 10 % HCl, brine, and dried over  $\text{MgSO}_4$ . Flash chromatography of the residue afforded 0.20 g of desired product  
 15635 (64%). NMR( $\text{CDCl}_3$ ) 7.80-7.85 (m, 2H); 7.28-7.32 (m, 2H); 6.9-7.0 (m, 1H); 4.9-5.0 (m, 1H); 4.60 (s, 2H); 3.80 (s, 3H); 3.68 (s, 3H); 2.35-2.45 (m, 2H); 2.12-2.35 (m, 1H); 2.1-2.2 (m, 1H). (DSI/ $\text{NH}_3$ )/MS: 316(M+H) $^+$ ; 333(M+ $\text{NH}_4$ ) $^+$ .

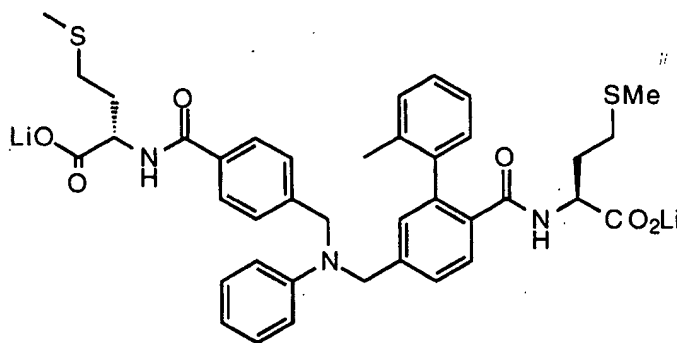


15640

Example 1246B

N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dimethyl ester

Prepared according to the procedure of example 1236A from the reaction between 1236C and 1246A. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.75-7.80 (m, 2H); 7.18-7.35 (m, 9H); 7.10 (s, 1H); 6.9-6.95 (m, 1H); 6.68-6.78 (m, 3H); 5.8-5.9 (m, 1H); 4.81 (s, 2H); 4.5-4.65 (m, 1H); 3.80 (s, 3H); 3.68 (s, 3H); 2.35-2.45 (m, 2H); 2.12-2.35 (m, 1H); ; 2.0-2.15 (m, 9H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 742(M+H)<sup>+</sup>.

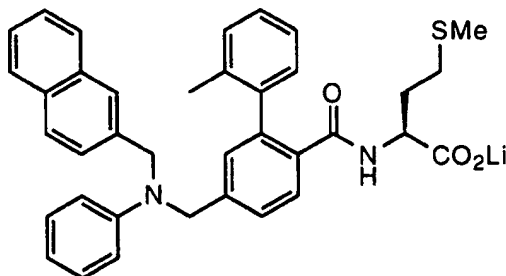


15650

Example 1246C

N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.

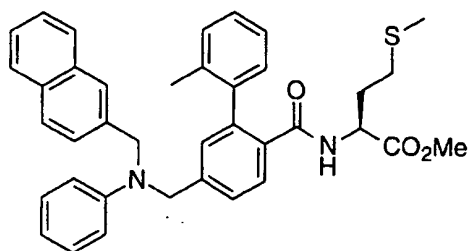
Prepared according to the procedure of example 1178J from 1246B. NMR <sup>1</sup>H (d<sub>4</sub>-MeOH): 7.8-7.9 (2H, m); 7.6-7.7 (1H, m); 7.3-7.4 (4H, m); 7.2 (4H, m); 7.1 (4H, m); 6.7-6.75 (2H, m); 6.6-6.7 (1H, m); 4.8 (4H, m); 4.5-4.6 (1H, m); 4.2-4.3 (1H, m); (2.5-2.65 (2H, m); 1.6-2.3 (15H, m). ESI(-)/MS: 711 (M-Li); 733 (M+Na-2H).



15660

Example 1247

N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



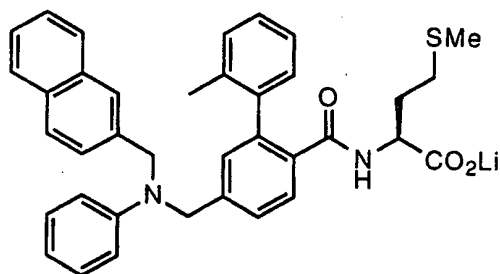
15665

Example 1247A

N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 2-bromomethyl-naphthalene. NMR(CDCl<sub>3</sub>) 7.68-7.95 (m, 5H); 7.18-7.45 (m, 11H); 7.1 (s, 1H); 6.7-6.85 (m, 3H); 5.8-5.9 (m, 1H); 4.80 (s, 2H); 4.76 (s, 2H); 4.56-4.7 (m, 1H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 603(M+H)<sup>+</sup>.

15670



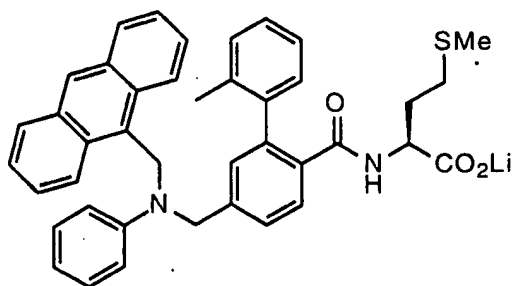
15675

Example 1247B

N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1247A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.78-7.84 (2H, m); 7.6-7.8 (3H, m), 7.3-7.5 (4H, d); 7.0-7.25 (8H, m); 6.8-7.0 (2H, m); 6.75-6.82 (2H, m); 6.6-6.6 (1H, m); 4.8 (2H, s); 4.85 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 587(M-Li).

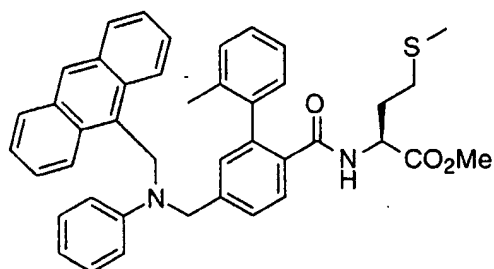
15680



15685

Example 1248

*N*-[4-*N*-(*N*-phenyl-*N*-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



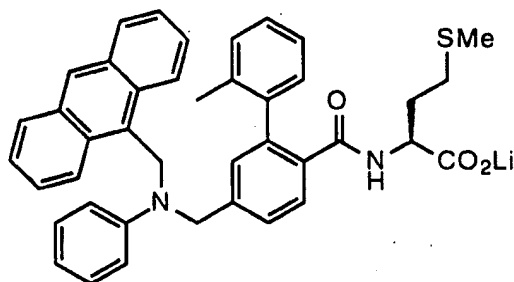
15690

Example 1248A

*N*-[4-*N*-(*N*-phenyl-*N*-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between

15695 1236C and 9-bromomethyl-anthracene. NMR(CDCl<sub>3</sub>) 8.4 (s, 1H); 8.1-8.2 (m, 2H); 7.9-8.0 (m, 2H); 7.0-7.65 (m, 12H); 7.1 (s, 1H); 6.8-6.95 (m, 3H); 5.8-5.9 (m, 1H); 5.45 (s, 2H); 4.68 (m, 1H); 4.25 (s, 2H); 3.60 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 653(M+H)<sup>+</sup>.



15700

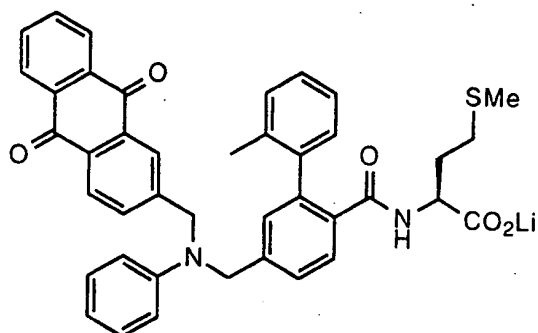
Example 1248B

*N*-[4-*N*-(*N*-phenyl-*N*-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1248A. NMR

15705 <sup>1</sup>H(MeOH-d<sub>4</sub>): 8.45 (1H, s); 8.17-8.22 (2H, m), 7.9-8.05 (2H, m); 7.1-7.5 (13H, m),

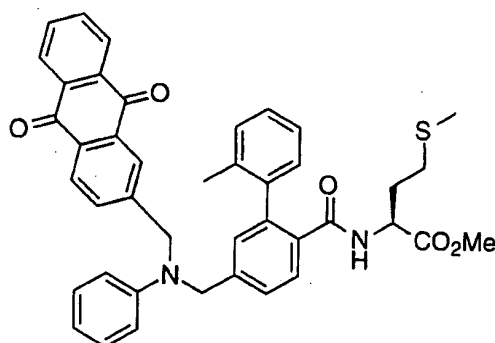
6.8-6.95 (3H, m); 6.5-6.67 (1H, m); 5.45 (2H, s); 4.5 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 637(M-Li).



15710

Example 1249

N-[4-N-(N-phenyl-N-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



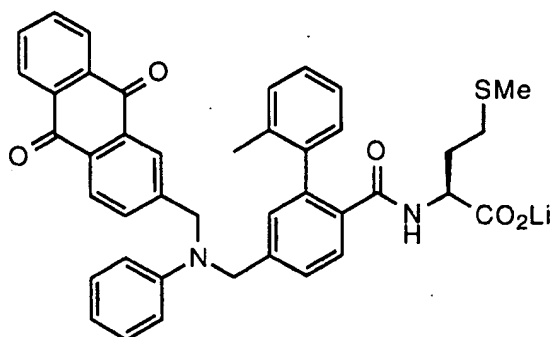
15715

Example 1249A

N-[4-N-(N-phenyl-N-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 2-bromomethyl-anthraquinone. NMR(CDCl<sub>3</sub>) 8.4 (s, 1H); 8.0-8.35 (m, 3H); 7.9-8.0 (m, 2H); 7.0-7.65 (m, 11H); 6.8-6.95 (m, 3H); 5.8-5.9 (m, 1H); 4.8 (s, 2H); 4.78 (s, 2H); 4.56-4.7 (m, 1H); 3.63 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 683(M+H)<sup>+</sup>.

15720

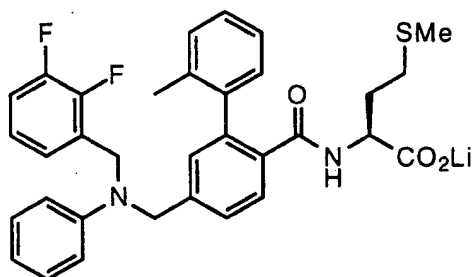


15725

**Example 1249B**

*N*-[4-*N*-(*N*-phenyl-*N*-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

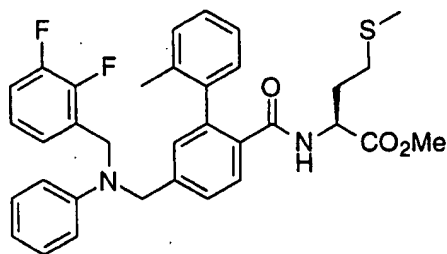
Prepared according to the procedure of example 1178J from 1249A. NMR  
 15730  $^1\text{H}$ (MeOH- $d_4$ ): 8.1-8.3 (4H, m); 7.8-7.9 (2H, m), 7.7-7.8 (1H, m); 7.6-7.7 (1H, m);  
 7.25-7.35 (1H, m); 7.0-7.3 (8H, m); 6.75-6.8 (2H, m); 6.6-6.7 (1H, m); 4.9 (2H, s); 4.8  
 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 667(M-Li).



15735

**Example 1250**

*N*-[4-*N*-(*N*-phenyl-*N*-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

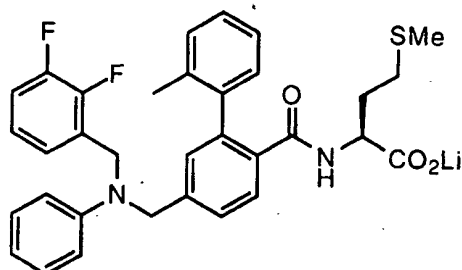


15740

**Example 1250A**

*N*-[4-*N*-(*N*-phenyl-*N*-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15745 Prepared according to the procedure of example 1236A from reaction between 1236C and 2,3-difluorobenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 6.95-7.40 (m, 11H); 6.68-6.8 (m, 3H); 5.8-5.9 (m, 1H); 4.75 (s, 2H); 4.70 (s, 2H); 4.60-4.70 (m, 1H); 3.70 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 589(M+H)<sup>+</sup>.

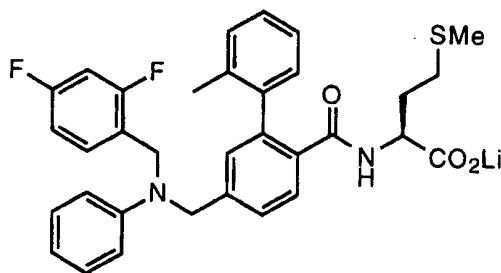


15750

Example 1250B

N-[4-N-(N-phenyl-N-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

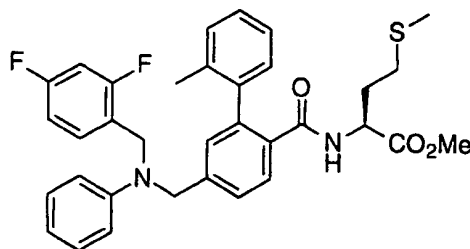
15755 Prepared according to the procedure of example 1178J from 1250A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.7-7.8 (1H, m); 7.3-7.4 (1H, m), 7.0-7.28 (11H, m); 6.65-6.75 (3H, m); 4.8-4.85 (4H, m); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 573(M-Li).



15760

Example 1251

N-[4-N-(N-phenyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt



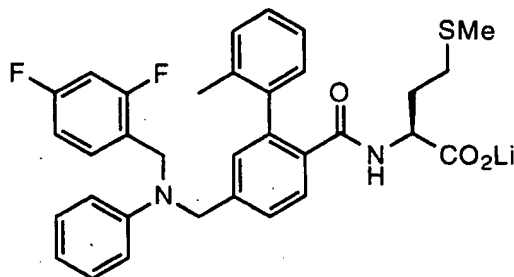


15765

Example 1251A

*N*-[4-*N*-(*N*-phenyl)-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

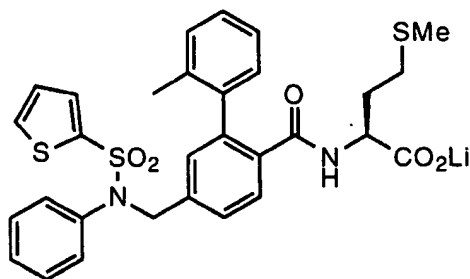
Prepared according to the procedure of example 1236A from reaction between 1236C and 2,4-difluorobenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.18-7.40 (m, 9H); 7.1 (s, 1H); 6.7-6.85 (m, 4H); 5.8-5.9 (m, 1H); 4.7 (s, 2H); 4.68 (m, 3H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 589(M+H)<sup>+</sup>.

Example 1251B

15775

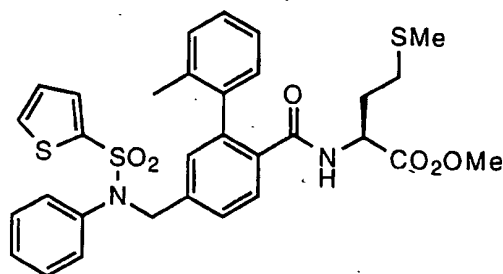
*N*-[4-*N*-(*N*-phenyl)-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1251A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.68 (1H, m); 7.3-7.4 (1H, m), 7.3-7.4 (1H, d); 7.0-7.3 (9H, m); 6.8-7.0 (2H, m); 6.6-6.8 (3H, m); 4.70 (2H, s); 4.75 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 573(M-Li).

Example 1255

15785

*N*-[4-*N*-(*N*-phenyl)-*N*-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

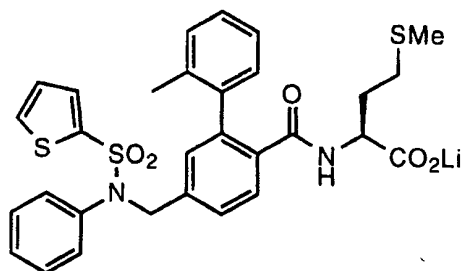
Example 1255A

15790

*N*-[4-*N*-(*N*-phenyl-*N*-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1229A from reaction between 1236C and 2-thiophenesulfonyl chloride. NMR(CDCl<sub>3</sub>) 7.75-7.82 (m, 1H); 7.60-7.62 (m, 1H); 7.39-7.42 (m, 1H); 7.12-7.38 (m, 9H); 7.05-7.11 (m, 2H); 6.95-7.05 (m, 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.5-4.65 (m, 1H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSL/NH<sub>3</sub>)/MS: 609(M+H)<sup>+</sup>; 626(M+NH<sub>4</sub>)<sup>+</sup>.

15795

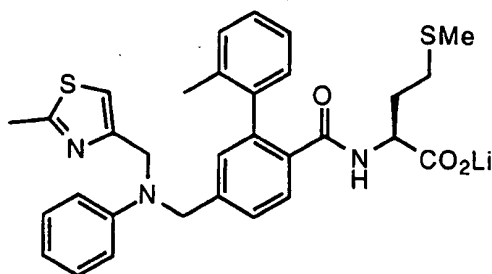
Example 1255B

15800

*N*-[4-*N*-(*N*-phenyl-*N*-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1255A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.8-7.9 (1H, m); 7.5-7.6 (1H, m), 7.42-7.45 (1H, m); 7.1-7.3 (9H, m); 6.95-7.1 (3H, m); 4.9 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 593(M-Li).

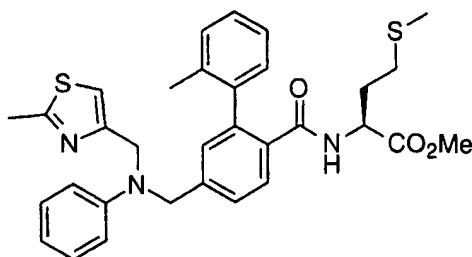
15805



Example 1256

15810

*N*-[4-*N*-(*N*-phenyl-*N*-(2-methyl-4-methylenethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

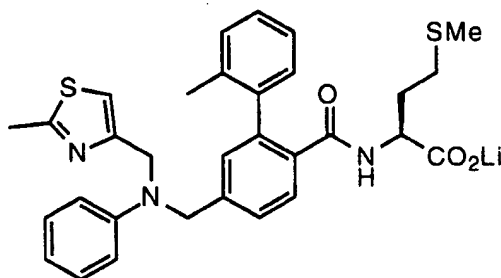
Example 1256A

15815

*N*-[4-*N*-(*N*-phenyl-*N*-(2-methyl-4-methylenethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1236C and 4-methyl-2-(bromomethyl)-thiazole. NMR(CDCl<sub>3</sub>) 7.82-7.95 (m, 1H); 7.10-7.40 (m, 9H); 6.8 (s, 1H); 6.7-6.8 (m, 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.75 (s, 2H); 4.56-4.7 (m, 1H); 3.68 (s, 3H); 2.67 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 574(M+H)<sup>+</sup>.

15820

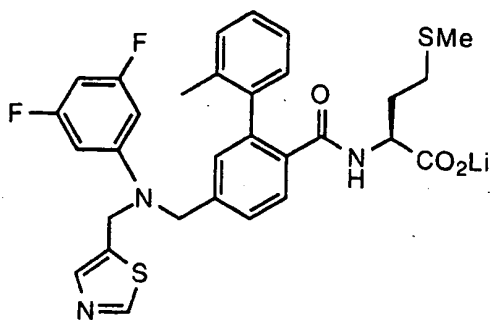
Example 1256B

15825

*N*-[4-*N*-(*N*-phenyl-*N*-(2-methyl-4-methylenethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

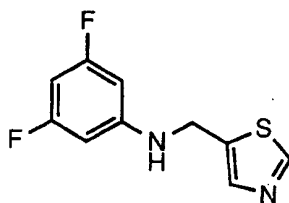
Prepared according to the procedure of example 1178J from 1256A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.68 (1H, m); 7.32-7.4 (1H, m), 7.0-7.28 (9H, m); 6.7-6.8 (2H, m); 6.6-6.7 (1H, m); 4.78 (2H, s); 4.70 (2H, s); 4.1-4.22 (1H, m); 2.62 (3H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 558(M-Li).

15830

Example 1257

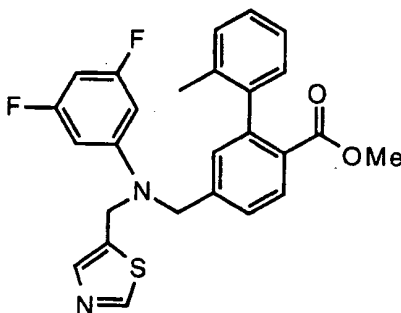
15835

N-[4-N-(N-3,5-difluorophenyl-N-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Example 1257A

15840

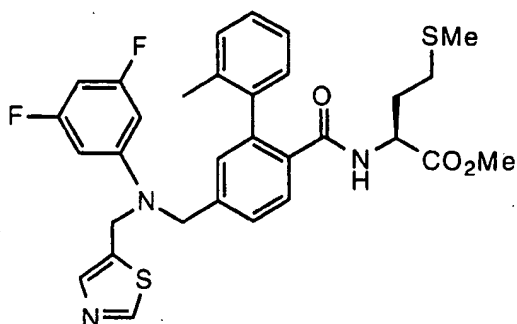
Prepared according to the procedure of example 1258A from reaction between 3,5-difluoroaniline and 5-thiazolecarboxaldehyde. NMR(CDCl<sub>3</sub>) 8.85 (s, 1H); 7.82 (s, 1H); 6.10-6.30 (m, 3H); 4.56 (s, 2H); 4.05-4.50 (m, 1H). DSI/NH<sub>3</sub>/MS: 227(M+H)<sup>+</sup>; 244(M+NH<sub>4</sub>)<sup>+</sup>.

Example 1257B

15845

Prepared according to the procedure of example 1287B from reaction between 1257A and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR(CDCl<sub>3</sub>) 8.75-8.80 (s, 1H); 7.82-8.00 (m, 1H); 7.75 (s, 1H); 7.12-7.38 (m, 4H); 7.00-7.10 (m, 2H); 6.20-6.27 (m, 3H); 4.80 (s, 2H); 4.60 (s, 2H); 3.60 (s, 3H); 2.03 (s, 3H). DSI/NH<sub>3</sub>/MS: 465(M+H)<sup>+</sup>; 482(M+NH<sub>4</sub>)<sup>+</sup>.

15850

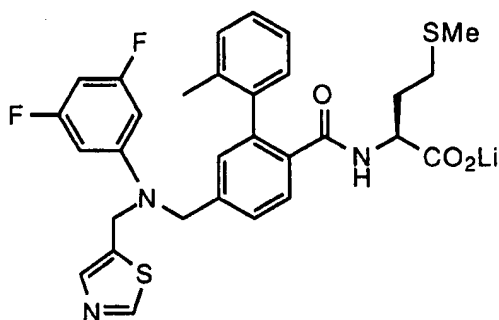
Example 1257C

15855

*N*-[4-*N*-(*N*-3,5-difluorophenyl)-*N*-(5-thiazolylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

Prepared according to the procedure of example 1258C from 1257B. NMR(CDCl<sub>3</sub>) 8.75-8.80 (s, 1H); 7.80-7.90 (m, 1H); 7.65-7.80 (m, 1H); 7.12-7.38 (m, 5H); 6.93 (s, 1H); 6.10-6.20 (m, 3H); 4.68 (s, 2H); 4.48-4.60 (m, 3H); 3.57 (s, 3H); 1.90-2.10 (m, 8H); 1.60-1.90 (m, 1H); 1.45-1.60 (m, 1H). DSI/NH<sub>3</sub>/MS: 596(M+H)<sup>+</sup>.

15860

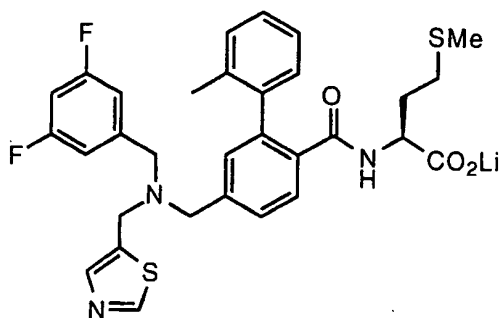
Example 1257D

15865

*N*-[4-*N*-(*N*-3,5-difluorophenyl)-*N*-(5-thiazolylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1257C. <sup>1</sup>H NMR (MeOH-d<sub>4</sub>): 8.9 (1H, s); 7.8 (1H, s); 7.6-7.7 (1H, m); 7.3-7.4 (1H, m); 7.1-7.3 (3H, m); 7.0-7.1 (1H, s); 6.3-6.45 (2H, m); 6.2-6.3 (1H, s); 4.95 (2H, s); 4.7 (2H, s); 4.1-4.22 (1H, m); 1.6-2.2 (10H, m). ESI(-)/MS: 580(M-Li). Anal. Calcd for C<sub>30</sub>H<sub>28</sub>F<sub>2</sub>N<sub>3</sub>O<sub>3</sub>S<sub>2</sub>Li•1.73H<sub>2</sub>O: C, 58.23; H, 5.12; N, 6.79. Found: C, 58.24; H, 4.90; N, 6.54.

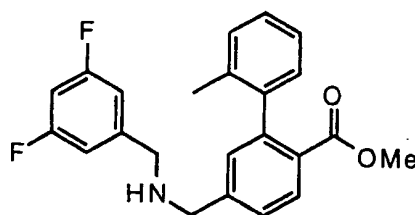
15870



15875

Example 1258

N-[4-N-(N-(5-thiazolylmethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

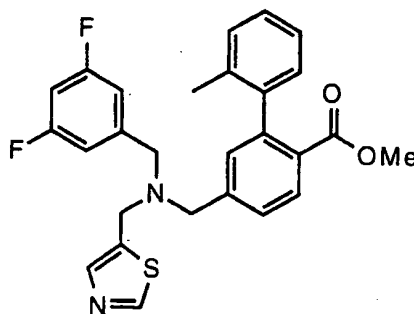


15880

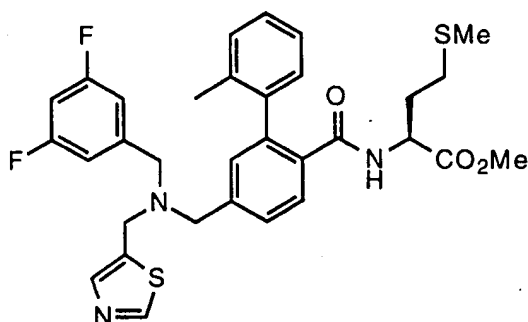
Example 1258A

A mixture of 3,5-difluorobenzyl amine (2.0 g, 14.2 mmol), 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester (3.6 g, 14.2 mmol), and sodium triacetoxyborohydride (6.0 g, 28.8 mmol) in 50 ml of 1,2-dichloroethane was stirred for 24 hours. The reaction mixture was washed with 4N NaOH and with brine, then dried over anhydrous MgSO<sub>4</sub>. Flash chromatography of the residue from evaporation of the organic solution eluting with 1:1 EtOAc/Hexane afforded 4.01 g of the title compound. (74%). NMR(CDCl<sub>3</sub>) 7.95-8.00 (m, 1H); 7.38-7.45 (m, 1H); 7.18-7.30 (m, 4H); 7.05-7.15 (m, 1H); 6.85-6.92 (m, 2H); 6.63-6.72 (m, 1H); 3.88 (s, 2H); 3.80 (s, 2H); 3.62 (s, 3H); 2.05 (s, 3H). (ESI/NH<sub>3</sub>)/MS: 382(M+H)<sup>+</sup>; 399(M+NH<sub>4</sub>)<sup>+</sup>.

15890

Example 1258B

Prepared according to the procedure of example 1258A from reaction between 1258A and 5-thiazolealdehyde. NMR(CDCl<sub>3</sub>) 8.80 (s, 1H); 7.95-8.00 (m, 1H); 7.72 (s, 1H); 7.50-7.55 (m, 1H); 7.10-7.32 (m, 4H); 7.0-7.1 (m, 1H); 6.9-7.0 (m, 2H); 6.68-6.72 (m, 1H); 4.62-4.70 (m, 2H); 3.60 (s, 5H); 2.07 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 479(M+H)<sup>+</sup>; 496(M+NH<sub>4</sub>)<sup>+</sup>.

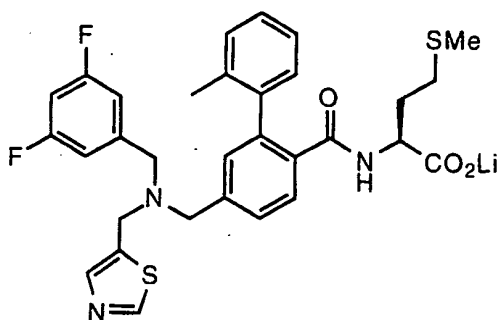


#### Example 1258C

A mixture of 1258B (0.304 g, 0.63 mmol) and lithium hydroxide (0.076 g, 3.15 mmol) in 30 ml of 1:1 water/methanol was refluxed for 12 hours. After cooling to room temperature, the reaction mixture was neutralized to PH= 5-6 carefully by 1.0 M NaHSO<sub>4</sub>. The precipitate from neutralization was extracted into 40 ml of EtOAc. The organic solution was then washed by brine, and dried over anhydrous MgSO<sub>4</sub>. Evaporation of the solvent afforded pure corresponding acid which was used directly for methionine-coupling reaction.

A mixture of the acid(0.30g, 0.63 mmol) from previous step, L-methionine methyl ester hydrochloride (0.252g, 1.26 mmol), 1-hydroxybenzotriazole hydrate (0.43 g, 3.15 mmol), 1-ethyl-3-(3-dimethyl-aminopropyl)carbodiimide (0.61 g, 3.15 mmol), and triethylamine hydrochloride (0.43 g, 3.15 mmol) in 15 ml of anhydrous DMF was heated under N<sub>2</sub> at 75°C for 20 hours. After cooling to room temperature, the solution was diluted with 50 ml of EtOAc, then was put to 200 ml of water. The aqueous solution was extracted with another portion of 50 ml of EtOAc. Combined organic solution was washed with 30 ml of saturated NaHCO<sub>3</sub> twice, then with 50 ml of brine, finally dried over anhydrous MgSO<sub>4</sub>. Flash chromatography of the residue from evaporation of the EtOAc solution eluting with 70:30 EtOAc/Hexane afforded 0.235 g of the title compound. (61%).

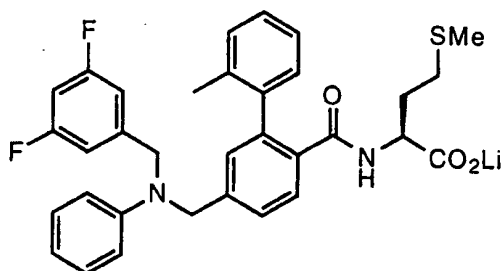
NMR(CDCl<sub>3</sub>) 8.78 (s, 1H); 7.90-8.00 (m, 1H); 7.72 (s, 1H); 7.50-7.55 (m, 1H); 7.20-7.38 (m, 5H); 6.9-7.0 (m, 2H); 6.68-6.72 (m, 1H); 5.88-5.92 (m, 2H); 4.58-4.70 (m, 1H); 3.88 (s, 2H); 4.62-4.70 (m, 5H); 3.60 (s, 2H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 610(M+H)<sup>+</sup>.

Example 1258D

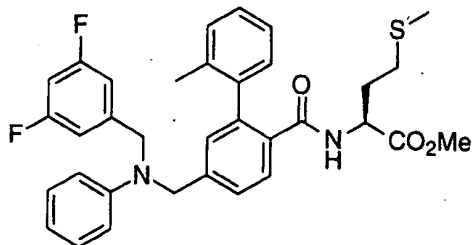
N-[4-N-(N-(5-thiazolylmethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example of 1178J from example 1258C.

NMR  $^1\text{H}$ (MeOH- $d_4$ ): 8.95 (1H, s); 7.78 (1H, s); 7.6-7.7 (1H, m); 7.4-7.5 (1H, m), 7.05-7.3 (5H, m); 6.95-7.05 (2H, m); 6.85-6.95 (1H, m); 4.95 (2H, s); 4.1-4.22 (1H, m); 3.9 (2H, s); 4.7 (2H, m); 4.6 (2H, s); 2.25 (2H, s); 1.6-2.1 (8H, m). ESI(-)/MS: 594(M-Li).

Example 1259

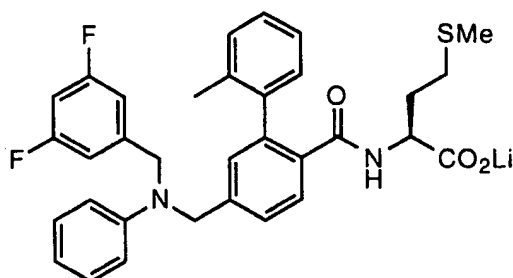
N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Example 1259A

N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester



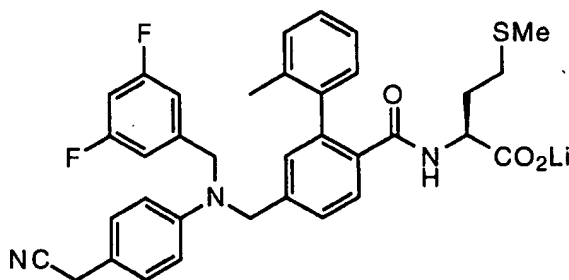
Prepared according to the procedure of example 1236A from reaction between 1236C and 3,5-difluorobenzyl bromide. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.18-7.40 (m, 9H); 7.1 (s, 1H); 6.75-6.8 (m, 2H); 6.65-6.75 (m, 2H); 5.8-5.9 (m, 1H); 4.7 (s, 2H); 4.6 (m, 3H); 3.68 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 589(M+H)<sup>+</sup>.



#### Example 1259B

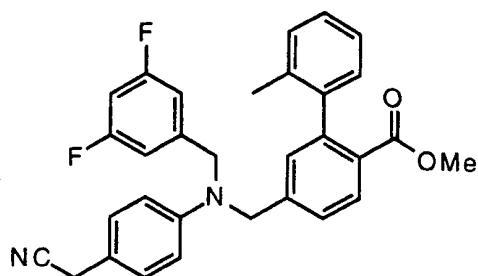
N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from 1259A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.7-7.8 (1H, m); 7.3-7.4 (1H, d), 7.0-7.3 (7H, d); 6.8-6.9 (3H, m); 6.6-6.8 (4H, m); 4.88 (2H, s); 4.85 (2H, s); 4.1-4.22 (1H, m); 1.7-2.1 (10H, m). ESI(-)/MS: 573(M-Li).



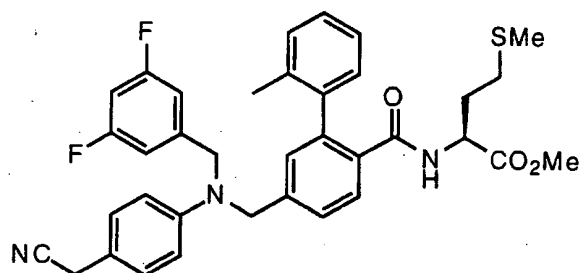
#### Example 1260

N-[4-N-(N-(4-acetonitrilephenyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Example 1260A

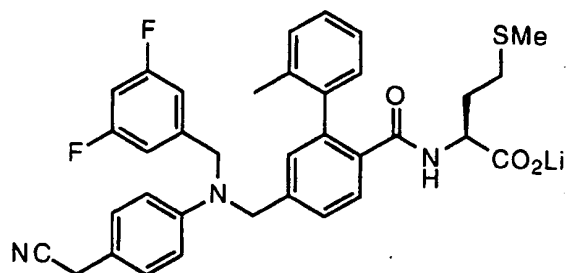
15965 Prepared according to the procedure of example 1236A from reaction 3,5-difluorobenzyl bromide, 4-bromomethyl-2-(2-methylphenyl)benzoic methyl ester, and 4-aminobenzyl cyanide. NMR(CDCl<sub>3</sub>) 7.95-8.00 (m, 1H); 7.02-7.35 (m, 8H); 6.62-6.80 (m, 5H); 4.75 (s, 2H); 4.65 (s, 2H); 3.65 (s, 2H); 3.60 (s, 3H); 2.01 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 497(M+H)<sup>+</sup>; 514(M+NH<sub>4</sub>)<sup>+</sup>.

15970

Example 1260B

N-[4-N-(N-(4-acetonitrilephenyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

15975 Prepared according to the procedure of example 1258C from example 1260A. NMR(CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.05-7.38 (m, 7H); 7.05 (s, 1H); 6.6-6.80 (m, 5H); 5.80-5.90 (m, 1H); 4.70 (s, 2H); 4.60 (s, 2H); 3.65 (s, 2H); 3.61 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 628(M+H)<sup>+</sup>; 645(M+NH<sub>4</sub>)<sup>+</sup>.

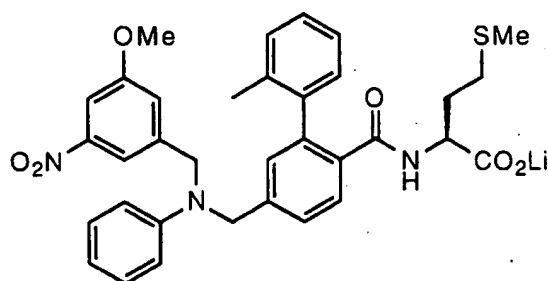


15980

Example 1260C

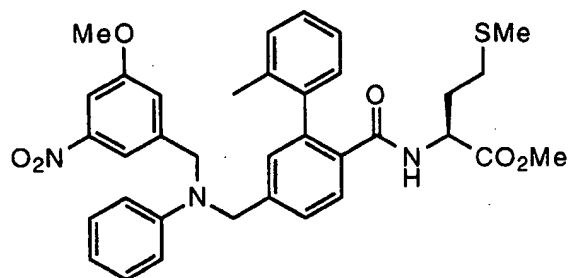
N-[4-N-(N-(4-acetonitrilephenyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from example 1260B. NMR  
<sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.3-7.4 (1H, m), 7.0-7.3 (8H, m); 6.65-6.9 (5H, m);  
 4.78 (2H, s); 4.7 (3H, s); 4.1-4.22 (1H, m); 3.7 (2H, s); 1.7-2.1 (10H, m). ESI(-)/MS:  
 612(M-Li). Anal. Calcd for C<sub>35</sub>H<sub>32</sub>F<sub>2</sub>N<sub>3</sub>O<sub>3</sub>SLi•1.64 H<sub>2</sub>O: C, 64.76; H, 5.48; N, 6.47.  
 Found: C, 64.75; H, 5.19; N, 6.16.



Example 1261

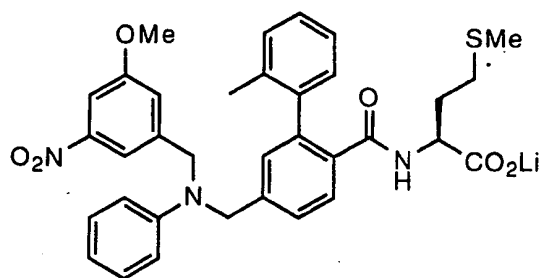
N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1261A

N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between  
 1236C and 3-methoxy-5-nitrobenzyl bromide. NMR(CDCl<sub>3</sub>) 8.1-8.2 (m, 2H); 8.0 (s, 1H);  
 7.68-7.95 (m, 1H); 7.1-7.40 (m, 8H); 6.9-6.95 (m, 1H); 6.7-6.8 (m, 1H); 6.6-6.7 (m,  
 2H); 5.8-5.9 (m, 1H); 4.78 (s, 2H); 4.6 (m, 3H); 3.92 (s, 3H); 3.68 (s, 3H); 2.0-2.15 (m,  
 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (ESI/NH<sub>3</sub>)/MS: 628(M+H)<sup>+</sup>.



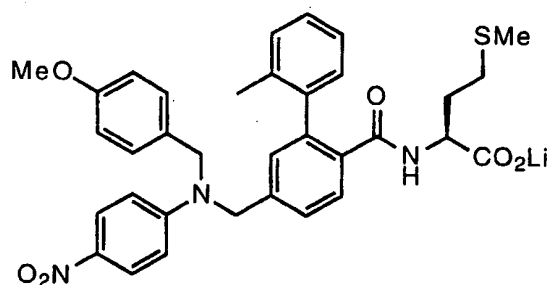
16005

Example 1261B

N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1261A. NMR

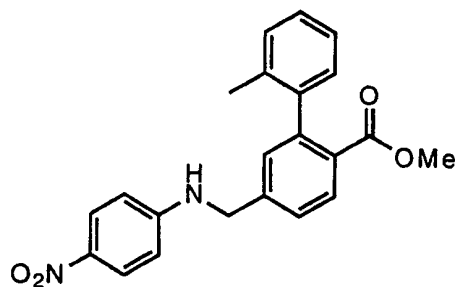
16010  $^1\text{H}$ (MeOH- $d_4$ ): 8.1-8.2 (1H, m); 7.9-8.0 (1H, m); 7.6-7.7 (1H, m); 7.3-7.4 (1H, m); 7.0-7.3 (9H, m); 6.6-6.75 (3H, m); 4.8(2H, s); 4.72 (2H, s); 4.1-4.22(1H, m); 3.95 (3H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 612(M-Li).



16015

Example 1262

N-[4-N-(N-(4-nitrophenyl)-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

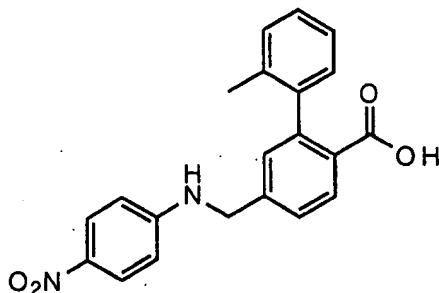


16020

Example 1262A

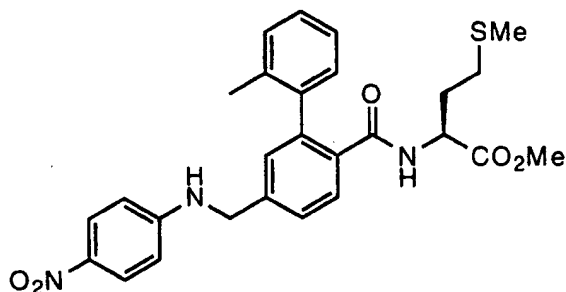
Prepared according to the procedure of example 1236A. Instead of using aniline, 4-nitroaniline was used to make the title compound. NMR( $\text{CDCl}_3$ ) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.24 (m, 5H); 7.0-7.18 (m, 1H); 6.55-6.60 (m,

16025 2H); 4.95 (m, 1H); 4.52 (s, 2H); 3.60 (s, 3H); 2.00 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 394(M+NH<sub>4</sub>)<sup>+</sup>.



Example 1262B

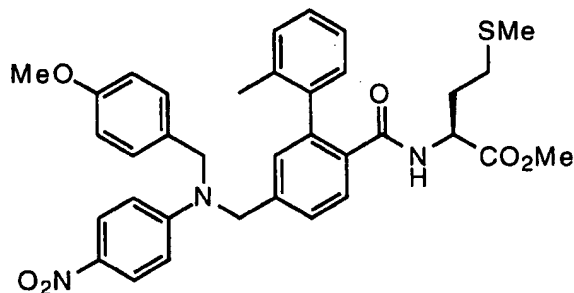
16030 Prepared according to the procedure of example 1178H from 1262A. NMR(CDCl<sub>3</sub>) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.18-7.24 (m, 5H); 7.0-7.18 (m, 1H); 6.55-6.60 (m, 2H); 4.95 (m, 1H); 4.52 (s, 2H); 2.00 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 380(M+NH<sub>4</sub>)<sup>+</sup>.



16035

Example 1262C

Prepared according to the procedure of example 1178I from 1262B. NMR(CDCl<sub>3</sub>) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.20-7.38 (m, 5H); 7.18-7.20 (m, 1H); 6.55-6.60 (m, 2H); 5.89-5.95 (m, 1H); 4.95-5.00 (m, 1H); 4.58-4.70 (m, 1H); 4.55 (m, 2H); 3.62 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 508(M+H)<sup>+</sup>; 525(M+NH<sub>4</sub>)<sup>+</sup>.

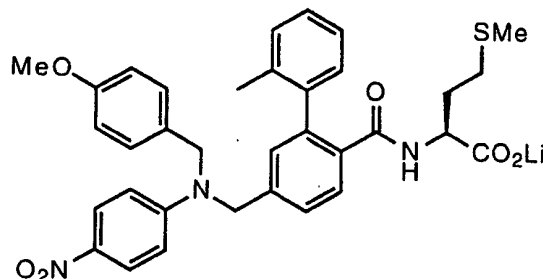


Example 1262D

16045

*N*-[4-*N*-(*N*-(4-nitrophenyl)-*N*-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1236A from reaction between 1262C and 4-methoxybenzyl bromide. NMR(CDCl<sub>3</sub>) 8.08-8.11 (m, 2H); 7.94-8.00 (m, 1H); 7.38-7.42 (m, 1H); 7.11-7.40 (m, 6H); 7.00 (m, 1H); 6.85-6.95 (m, 3H); 6.55-6.60 (m, 2H); 5.89-5.95 (m, 1H); 4.80 (s, 2H); 4.70(s, 2H); 4.60-4.70 (m, 1H); 3.80 (s, 3H); 3.67 (s, 3H); 2.0-2.15 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H). (DSI/NH<sub>3</sub>)/MS: 628(M+H)<sup>+</sup>.

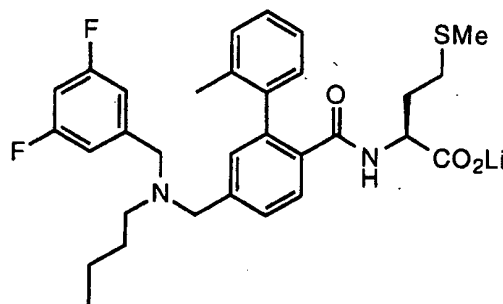


16055

Example 1262E

*N*-[4-*N*-(*N*-(4-nitrophenyl)-*N*-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

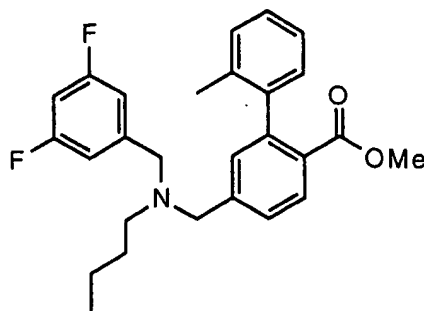
Prepared according to the procedure of example 1178J from 1262D. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 8.0-8.05 (2H, m); 7.4-7.5 (1H, m), 7.3-7.4 (1H, m); 7.18-7.3 (7H, m); 7.0 (1H, m); 6.8-6.9 (4H, m); 4.8-4.85 (4H, m); 4.1-4.22 (1H, m); 3.88 (3H, s); 1.7-2.1 (10H, m). ESI(-)/MS: 612(M-Li).



16065

Example 1263

*N*-[4-*N*-(*N*-butyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

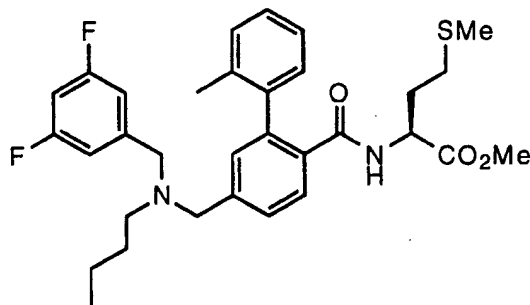


16070

Example 1263A

Prepared according to the procedure of example 1258A from reaction between 1258A and butyraldehyde. NMR(CDCl<sub>3</sub>) 7.92-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.10-7.32 (m, 4H); 7.0-7.1 (m, 1H); 6.8-6.95 (m, 2H); 6.60-6.75 (m, 1H); 3.58-3.63 (m, 5H); 3.55 (s, 2H); 2.38-2.48 (t, 2H); 2.07 (s, 3H); 1.4-1.6 (m, 2H); 1.2-1.4 (m, 2H); 0.8-0.9 (t, 3H). (DSI/NH<sub>3</sub>)/MS: 437(M+H)<sup>+</sup>.

16075

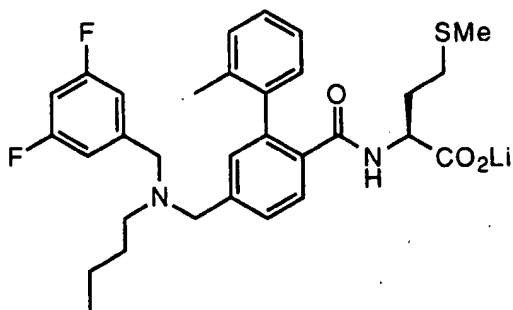
Example 1263B

N-[4-N-(N-butyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

16080

Prepared according to the procedure of example 1258C from 1263A. NMR(CDCl<sub>3</sub>) 7.9-8.00 (m, 1H); 7.40-7.46 (m, 1H); 7.20-7.40 (m, 4H); 7.20 (s, 1H); 6.7-6.85 (m, 2H); 6.60-6.75 (m, 1H); 5.82-5.92 (m, 1H); 4.58-4.70 (m, 1H); 3.65 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H); 2.40-2.48 (t, 2H); 2.20 (s, 3H); 1.8-1.96 (m, 1H); 1.55-1.65 (m, 1H); 1.45-1.55 (m, 2H); 1.2-1.4 (m, 2H); 0.8-0.9 (t, 3H). (DSI/NH<sub>3</sub>)/MS: 569(M+H)<sup>+</sup>.

16085

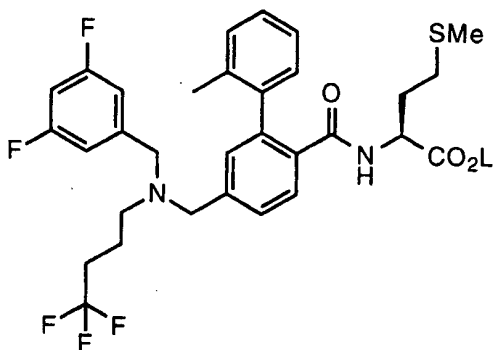


Example 1263C

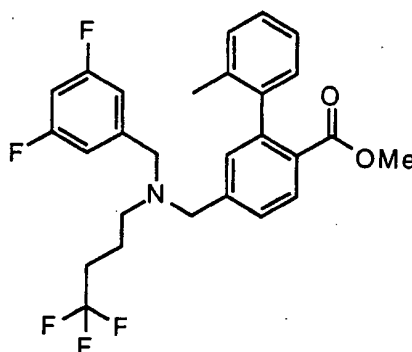
*N*-[4-*N*-(*N*-butyl-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1263B. NMR

<sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.65 (2H, s); 3.58 (2H, s); 2.4-2.5 (2H, m); 2.21 (1H, m); 1.8-2.1 (10H, m); 1.4-1.5 (2H, m); 1.22-1.4 (2H, m); 0.8-0.9 (3H, m). ESI(-)/MS: 553(M-Li). Anal. Calcd for C<sub>31</sub>H<sub>35</sub>F<sub>2</sub>N<sub>2</sub>O<sub>3</sub>SLi•1.5 LiOH•0.26H<sub>2</sub>O: C, 62.04; H, 6.05; N, 4.48. Found: C, 62.04; H, 6.05; N, 4.67.

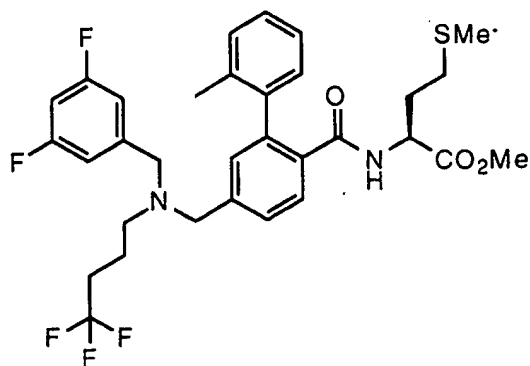
Example 1264

*N*-[4-*N*-(*N*-(4,4,4-trifluorobutyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Example 1264A

Prepared according to the procedure of example 1258A from reaction between 1258A and 4,4,4-trifluorobutylaldehyde. NMR(CDCl<sub>3</sub>) 7.92-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.10-7.32 (m, 4H); 7.0-7.1 (m, 1H); 6.8-6.92 (m, 2H); 6.62-6.78 (m, 1H); 3.58-3.63 (m, 5H); 3.55 (s, 2H); 2.43-2.55 (t, 2H); 2.00-2.1 (m, 5H); 1.7-1.82 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 492(M+H)<sup>+</sup>.



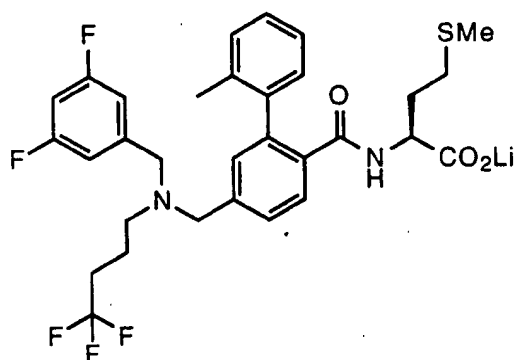
Example 1264B

N-[4-N-(N-(4,4,4-trifluorobutyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

16115

Prepared according to the procedure of example 1258C from 1264A. NMR(CDCl<sub>3</sub>) 7.9-8.00 (m, 1H); 7.40-7.46 (m, 1H); 7.20-7.40 (m, 4H); 7.20 (s, 1H); 6.7-6.85 (m, 2H); 6.60-6.75 (m, 1H); 5.82-5.92 (m, 1H); 4.58-4.70 (m, 1H); 3.65 (s, 3H); 3.61 (s, 2H); 3.55 (s, 2H); 2.40-2.48 (t, 2H); 1.5-2.16 (m, 14H). (ESI/NH<sub>3</sub>)/MS: 623(M+H)<sup>+</sup>.

16120

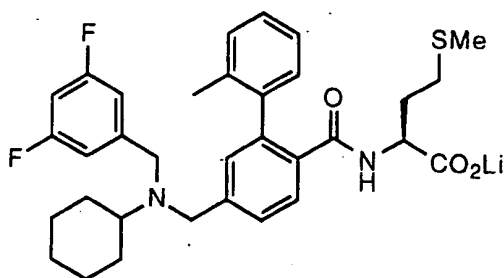
Example 1264C

N-[4-N-(N-(4,4,4-trifluorobutyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16125

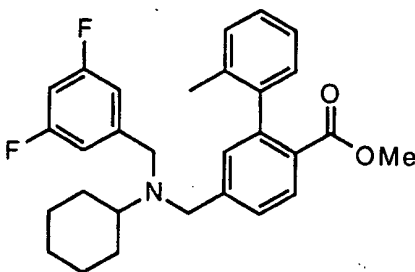
Prepared according to the procedure of example 1178J from 1264B. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.65 (2H, s); 3.6 (2H, s); 2.5-2.6 (2H, m); 1.6-2.25 (14H, m); 1.4-1.5 (2H, m); 1.22-1.4 (2H, m); 0.8-0.9 (3H, m). ESI(-)/MS: 609(M-Li). Anal. Calcd for C<sub>31</sub>H<sub>30</sub>F<sub>5</sub>N<sub>2</sub>O<sub>3</sub>SLi•1.21H<sub>2</sub>O: C, 58.70; H, 5.15; N, 4.42. Found: C, 58.69; H, 5.16; N, 4.18.

16130

Example 1265

16135

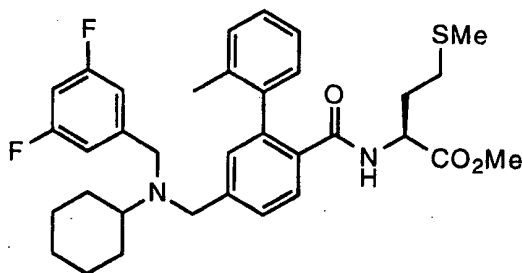
*N*-[4-*N*-(*N*-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Example 1265A.

16140

Prepared according to the procedure of example 1258A from reaction between 1258A and cyclohexanone. NMR (CDCl<sub>3</sub>) 7.90-7.95 (m, 1H); 7.40-7.45 (m, 1H); 7.18-7.38 (m, 4H); 7.00-7.09 (m, 1H); 6.84-6.94 (m, 2H); 6.58-6.68 (m, 1H); 3.68 (s, 2H); 3.62 (m, 5H); 2.40-2.50 (m, 1H); 2.08 (s, 3H); 1.75-1.96 (m, 4H); 1.05-1.65 (m, 6H). (DSI/NH<sub>3</sub>)/MS: 464(M+H)<sup>+</sup>.

16145

Example 1265B

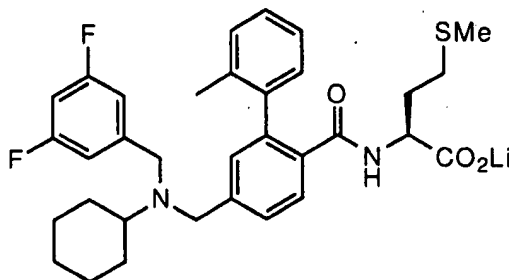
*N*-[4-*N*-(*N*-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine, methyl ester

16150

Prepared according to the procedure of example 1258C from 1265A. NMR (CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.38-7.45 (m, 1H); 7.18-7.38 (m, 4H); 7.2 (s, 1H); 6.84-6.94 (m, 2H); 6.58-6.68 (m, 1H); 5.85-5.93 (m, 1H); 4.56-4.65 (m, 1H); 3.70 (s, 2H); 3.65 (s,

2H); 3.61 (s, 3H); 2.40-2.50 (m, 1H); 1.96-2.18 (m, 7H); 1.71-1.96 (m, 6H); 1.55-1.68 (m, 1H); 1.05-1.52 (m, 6H). (DSI/NH<sub>3</sub>)/MS: 595(M+H)<sup>+</sup>.

16155



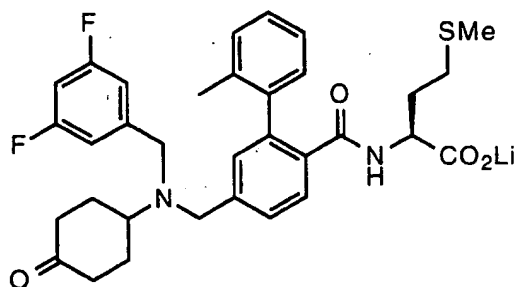
Example 1265C

N-[4-N-(N-cyclohexyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16160

Prepared according to the procedure of example 1178J from 1265B. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.35-7.45 (1H, m), 7.0-7.35 (5H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.7 (3H, s); 3.65 (3H, s); 2.4-2.52 (1H, m); 2.1 (1H, m); 1.7-2.1 (11H, m); 1.5-1.7 (2H, m); 1.23-1.5 (2H, m); 1.05-1.25 (3H, m). ESI(-)/MS: 579(M-Li).

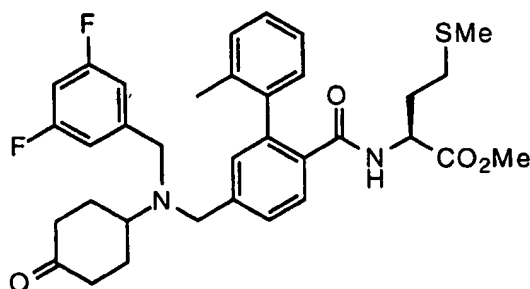
16165



Example 1266

N-[4-N-(N-(4-cyclohexanonyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16170



Example 1266A

*N*-[4-*N*-(*N*-(4-cyclohexanonyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

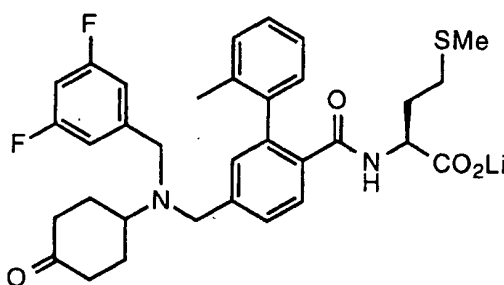
16175

A mixture of 1267B (0.42 g, 0.604 mmol) and 10 ml of 10% of HCl in 35 ml of acetone was refluxed until all 1267B disappeared. Solvents were removed under vacuum. The residue was treated with 20 ml of 2N Na<sub>2</sub>CO<sub>3</sub>, then extracted by 50 ml of EtOAc. The organic solution was then washed with brine, dried over anhydrous MgSO<sub>4</sub>. The crude

16180

product was purified by flash chromatography eluting with 1:1 EtOAc/Hexane to afford 0.25 g of the title compound. NMR (CDCl<sub>3</sub>) 7.82-7.95 (m, 1H); 7.40-7.49 (m, 1H); 7.18-7.40 (m, 5H); 6.82-6.92 (m, 2H); 6.58-6.68 (m, 1H); 5.82-5.91 (m, 1H); 4.58-4.68 (m, 1H); 3.61-3.75 (m, 7H); 2.95-3.05 (m, 1H); 1.5-2.5 (m, 18H). (DSI/NH<sub>3</sub>)/MS: 609(M+H)<sup>+</sup>; 626(M+NH<sub>4</sub>)<sup>+</sup>.

16185



Example 1266B

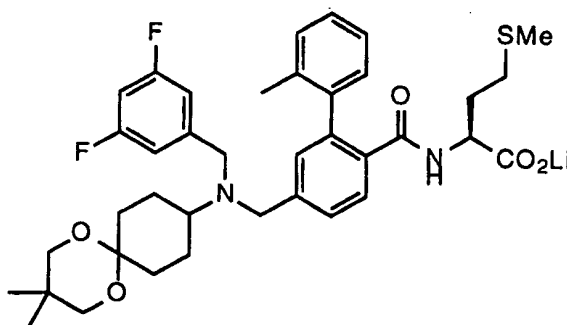
*N*-[4-*N*-(*N*-(4-cyclohexanonyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16190

Prepared according to the procedure of example 1178J from 1266A. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.4-7.5 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.75 (2H, s); 3.7 (2H, s); 2.1-2.3 (3H, m); 1.76-2.1 (14H, m); 1.5-1.78 (2H, m). ESI(-)/MS: 593(M-Li). Anal. Calcd for C<sub>33</sub>H<sub>35</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub>SLi•1.73H<sub>2</sub>O•1.5LiOH: C, 60.32; H, 5.95; N, 4.26. Found: C, 60.33;

16195

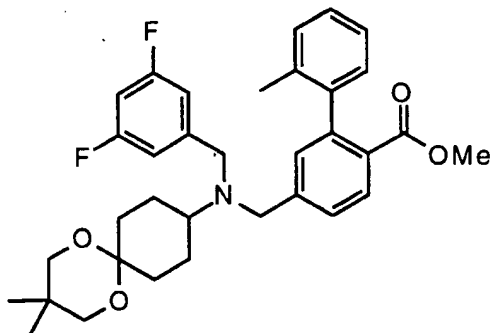
H, 5.62; N, 4.04.



Example 1267

16200

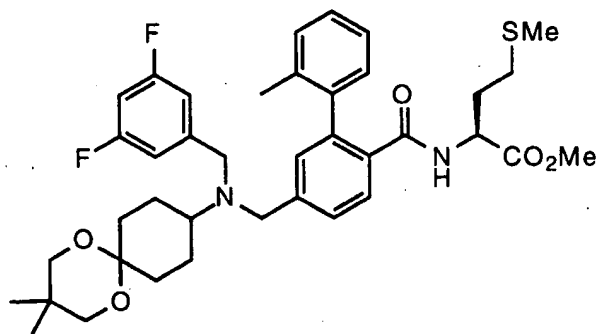
*N*-[4-*N*-(*N*-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Example 1267A

16205

Prepared according to the procedure of example 1258A from reaction between 1258A and 1,4-cyclohexanedione *mono*-2,2-dimethyltrimethylene ketal. NMR (CDCl<sub>3</sub>) 7.82-7.92 (m, 1H); 7.36-7.42 (m, 1H); 7.18-7.38 (m, 4H); 7.20 (s, 1H); 6.82-6.92 (m, 2H); 6.58-6.68 (m, 1H); 3.68 (s, 2H); 3.60 (s, 3H); 3.59 (s, 2H); 3.48 (s, 2H); 3.42 (s, 2H); 2.50-2.60 (m, 1H); 2.22-2.38 (m, 2H); 1.80-2.20 (m, 6H); 1.2-1.3 (m, 2H); 0.95 (s, 6H). (DSI/NH<sub>3</sub>)/MS: 564(M+H)<sup>+</sup>.

16210

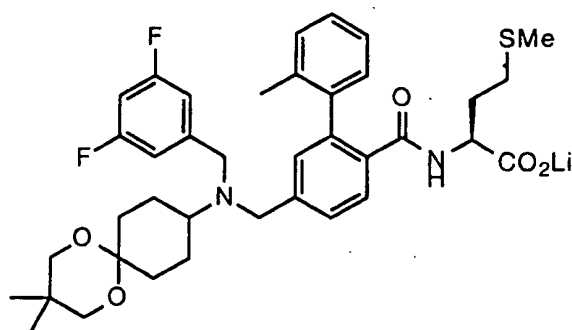
Example 1267B

16215

*N*-[4-*N*-(*N*-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1267A. NMR (CDCl<sub>3</sub>) 7.82-7.92 (m, 1H); 7.36-7.42 (m, 1H); 7.18-7.38 (m, 4H); 7.20 (s, 1H); 6.82-6.92 (m, 2H); 6.58-6.68 (m, 1H); 5.82-5.91 (m, 1H); 4.58-4.68 (m, 1H); 3.68 (s, 2H); 3.60 (s, 3H); 3.59 (s, 2H); 3.48 (s, 2H); 3.42 (s, 2H); 2.50-2.60 (m, 1H); 2.22-2.38 (m, 2H); 1.50-2.2 (m, 14H); 1.2-1.3 (m, 2H); 0.95 (s, 6H). (DSI/NH<sub>3</sub>)/MS: 695(M+H)<sup>+</sup>.

16220

Example 1267C

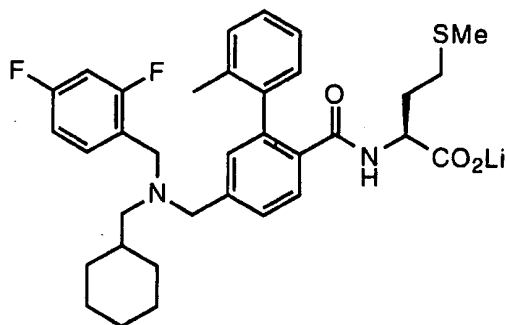
16225

*N*-[4-*N*-(*N*-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1267B. NMR

<sup>1</sup>H(MeOH-d<sub>4</sub>): 7.55-7.65 (1H, m); 7.38-7.48 (1H, m), 7.0-7.35 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.7 (2H, s); 3.65(2H, s); 3.45 (4H, s); 2.5-2.65 (1H, m); 2.26-2.4 (2H, m); 2.2 (1H, s); 1.5-2.1 (13H, m); 1.1-1.3 (2H, m); 0.95 (6H, s). ESI(-)/MS: 686.79(M-Li). Anal. Calcd for C<sub>38</sub>H<sub>45</sub>F<sub>2</sub>N<sub>2</sub>O<sub>5</sub>SLi•0.99H<sub>2</sub>O•1.0LiOH: C, 62.65; H, 6.64; N, 3.84. Found: C, 62.65; H, 6.33; N, 3.71.

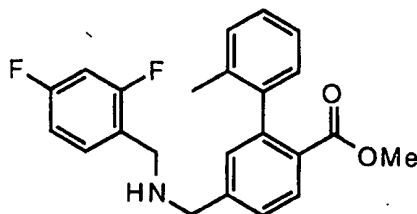
16230



16235

Example 1268

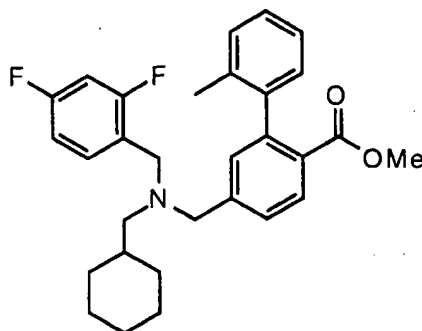
*N*-[4-*N*-(*N*-cyclohexylmethyl)-*N*-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



16240

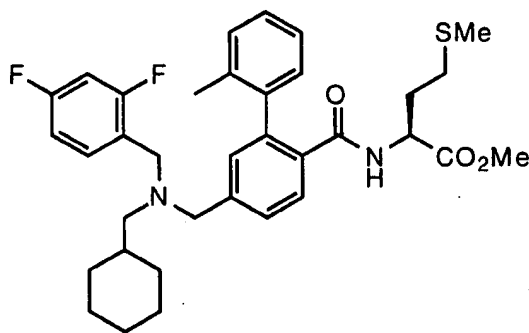
Example 1268A

Prepared according to the procedure of example 1258A from the reaction between 2,4-difluorobenzyl amine and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR (CDCl<sub>3</sub>) 7.22-7.30 (m, 2H); 6.85-6.90 (m, 3H); 3.88 (s, 2H); 2.40-2.45 (m, 2H); 1.6-1.8 (m, 5H); 1.38-1.60 (m, 2H); 1.05-1.40 (m, 3H); 0.8-1.0 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 240(M+H)<sup>+</sup>.



#### Example 1268B

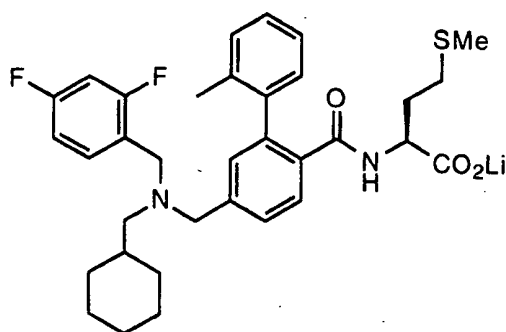
Prepared according to the procedure of example 1258A from reaction between 1268A and cyclohexanecarboxaldehyde. NMR (CDCl<sub>3</sub>) 7.90-7.95 (m, 1H); 7.38-7.47 (m, 2H); 7.20-7.35 (m, 4H); 7.0-7.10 (m, 1H); 6.75-6.85 (m, 2H); 3.60(s, 3H); 3.55 (s, 2H); 3.52 (s, 2H); 2.20-2.23 (m, 2H); 2.05 (s, 3H); 1.72-1.83 (m, 2H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 478(M+H)<sup>+</sup>.



#### Example 1268C

N-[4-N-(N-cyclohexylmethyl)-N-(2,4-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoylmethionine, methyl ester

Prepared according to the procedure of example 1258C from 1268B. NMR (CDCl<sub>3</sub>) 7.85-7.95 (m, 1H); 7.20-7.47 (m, 6H); 7.18 (s, 1H); 6.75-6.85 (m, 2H); 5.85-5.92 (m, 1H); 4.56-4.67 (m, 1H); 3.67(s, 3H); 3.57 (s, 2H); 3.55 (s, 2H); 2.18-2.23 (m, 4H); 2.00-2.11 (m, 6H); 1.72-1.83 (m, 3H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 609(M+H)<sup>+</sup>.

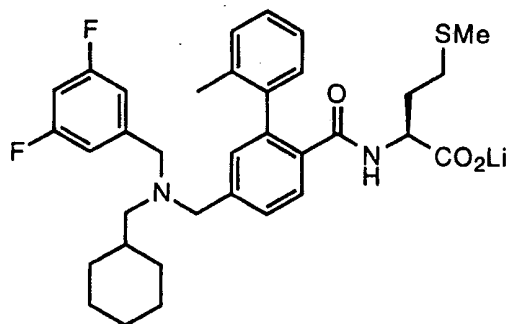
Example 1268D

N-[4-N-(N-cyclohexylmethyl)-N-(2,4-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16270

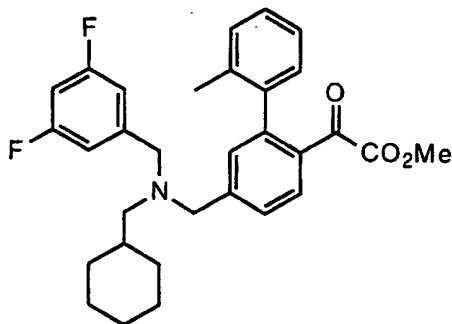
Prepared according to the procedure of example 1178J from 1267C. NMR  $^1\text{H}$ (MeOH- $d_4$ ): 7.6-7.7 (1H, m); 7.38-7.48 (2H, m), 7.0-7.28 (6H, m); 6.8-6.95 (2H, m); 4.1-4.22 (1H, m); 4.58 (4H, s); 2.2-2.3 (4H, m); 1.76-2.1 (9H, m); 1.5-1.78 (5H, m); 1.1-1.3 (3H, m); 0.7-0.82 (2H, m). ESI(-)/MS: 593(M-Li).

16275

Example 1269

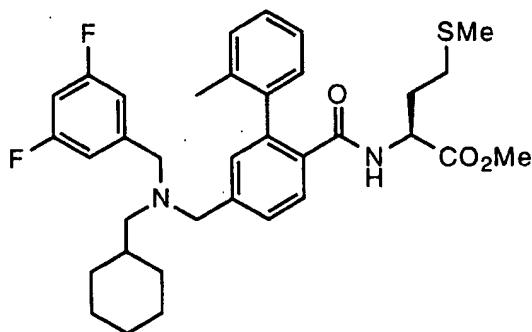
N-[4-N-(N-cyclohexylmethyl)-N-(3,5-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16280

Example 1269A



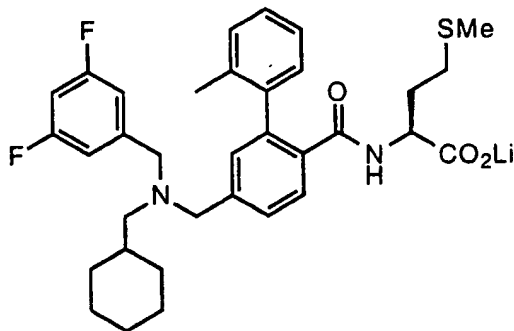
Prepared according to the procedure of example 1258A from reaction between 1258A and cyclohexanecarboxaldehyde. NMR (CDCl<sub>3</sub>) 7.95-8.05 (m, 1H); 7.40-7.47 (m, 1H); 7.15-7.35 (m, 5H); 7.04-7.11 (m, 1H); 6.75-6.85 (m, 2H); 6.60-6.70 (m, 1H); 3.60(s, 3H); 3.55 (s, 2H); 3.45 (s, 2H); 2.18-2.25 (m, 2H); 2.05 (s, 3H); 1.72-1.83 (m, 2H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 478(M+H)<sup>+</sup>.



#### Example 1269B

N-[4-N-(N-cyclohexylmethyl)-N-(3,5-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1269A. NMR (CDCl<sub>3</sub>) 7.79-7.95 (m, 1H); 7.40-7.48 (m, 1H); 7.20-7.41 (m, 5H); 7.18 (s, 1H); 6.75-6.85 (m, 2H); 6.60-6.70 (m, 1H); 5.85-5.92 (m, 1H); 4.56-4.67 (m, 1H); 3.67(s, 3H); 3.57 (s, 2H); 3.45 (s, 2H); 2.18-2.23 (m, 4H); 2.00-2.11 (m, 6H); 1.72-1.83 (m, 3H); 1.52-1.72 (m, 4H); 1.10-1.30 (m, 3H); 0.6-0.8 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 609(M+H)<sup>+</sup>.



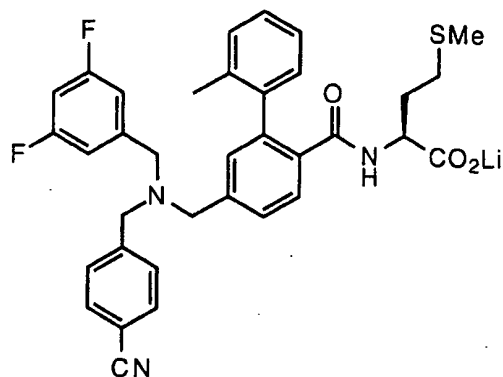
#### Example 1269C

N-[4-N-(N-cyclohexylmethyl)-N-(3,5-difluorobenzyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1269B. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.38-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 4.6 (2H, s); 4.55 (2H, s); 2.2-2.3 (4H, m); 1.76-2.1

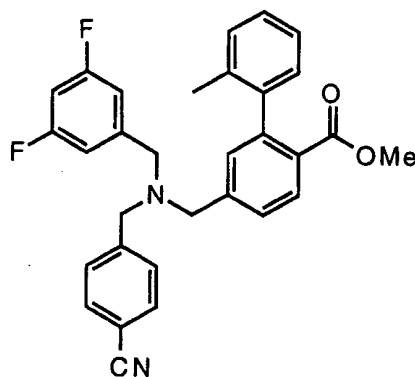
(9H, m); 1.5-1.78 (5H, m); 1.1-1.3 (3H, m); 0.7-0.82 (2H, m). ESI(-)/MS: 593(M-Li).  
 Anal. Calcd for  $C_{31}H_{30}F_5N_2O_3SLi \cdot 1.0LiOH$ : C, 65.38; H, 6.45; N, 4.48 Found: C, 65.43; H, 6.17; N, 4.40.

16310

Example 1270

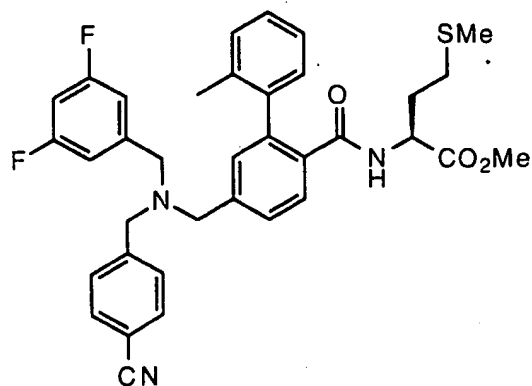
N-[4-N-(N-(4-cyanobenzyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16315

Example 1270A

Prepared according to the procedure of example 1258A from reaction between  
 1258A and 4-cyanobenzaldehyde. NMR(CDCl<sub>3</sub>) 7.95-8.00 (m, 1H); 7.60-7.65 (m, 2H);  
 7.40-7.56 (m, 3H); 7.20-7.38 (m, 4H); 7.00-7.10 (m, 1H); 6.85-6.95 (m, 2H); 6.65-6.75  
 (, 1H); 3.58-3.65 (m, 7H); 3.54-3.58 (m, 2H); 2.05 (s, 3H). (DSI/NH<sub>3</sub>)/MS: 585(M+H)+  
 ; 497 (M+NH<sub>4</sub>)+. 514 (M+NH<sub>4</sub>)+.

16320



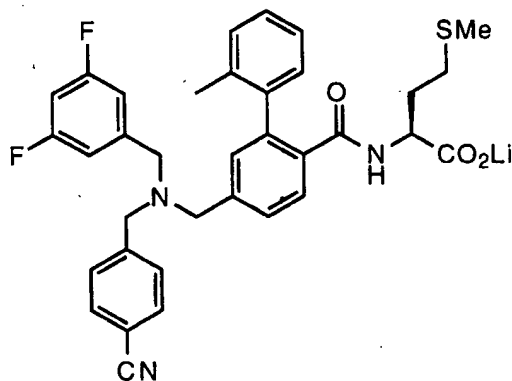
16325

**Example 1270B**

*N*-[4-*N*-(*N*-(4-cyanobenzyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1270A. NMR(CDCl<sub>3</sub>)

16330 8.00-8.18 (m, 1H); 7.76-7.80 (m, 2H); 7.48-7.76 (m, 3H); 7.10-7.38 (m, 5H); 7.00-7.11 (m, 2H); 6.80-6.85 (m, 1H); 5.95-6.05 (m, 1H); 4.70-4.81 (m, 1H); 3.70-3.90 (m, 9H); 3.54-3.58 (m, 2H); 1.95-2.20 (m, 8H); 1.7-2.0 (m, 1H); 1.5-1.7 (m, 1H).  
(DSI/NH<sub>3</sub>)/MS: 628(M+H)<sup>+</sup>; 645(M+NH<sub>4</sub>)<sup>+</sup>.



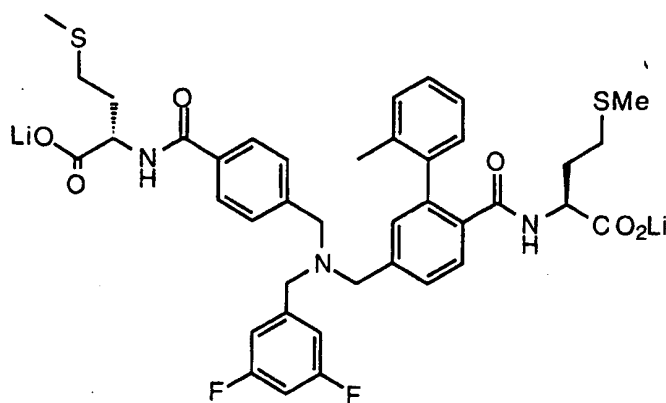
16335

**Example 1270C**

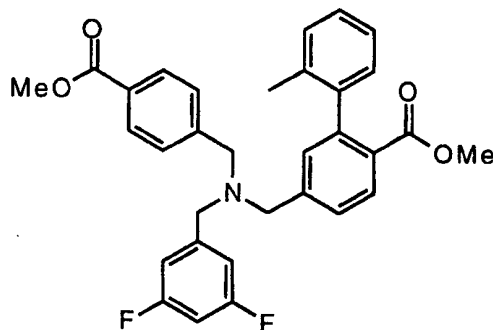
*N*-[4-*N*-(*N*-(4-cyanobenzyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1270B. NMR

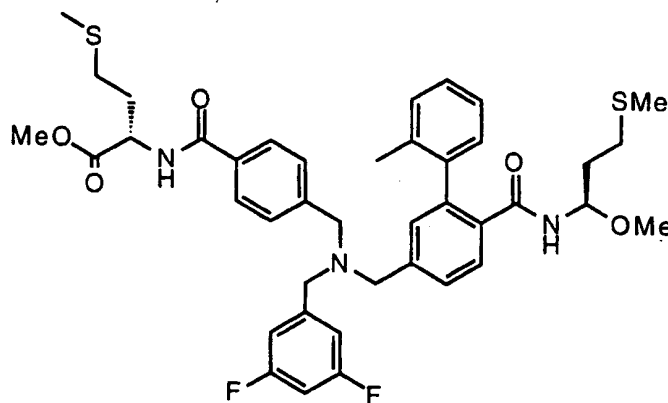
16340 <sup>1</sup>H(MeOH-d<sub>4</sub>): 8.78 (1H, s); 7.6-7.7 (2H, m); 7.5-7.6 (2H, m), 7.5-7.55 (1H, m); 7.0-7.3 (6H, m); 6.9-7.0 (2H, m); 6.77-6.82 (1H, m); 4.1-4.22 (1H, m); 3.7 (2H, s); 3.65 (2H, s); 3.6 (2H, s); 1.5-2.2 (10H, m).ESI(-)/MS: 612(M-Li).

**Example 1271**

*N*-[4-*N*-(*N*-(3,5-difluorobenzyl)-*N*-(4-*N*-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.

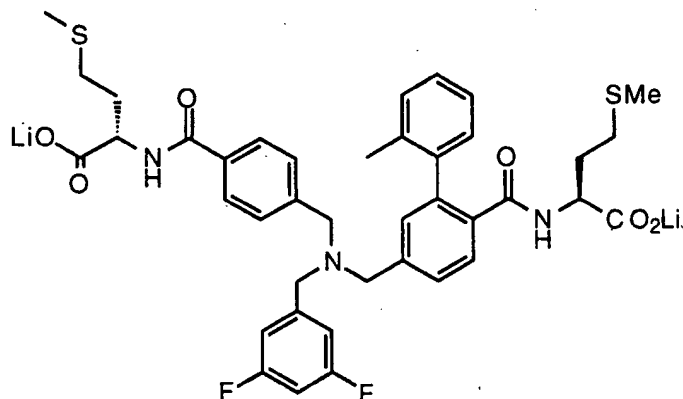
**Example 1271A**

Prepared according to the procedure of example 1236A from reaction between 1258A and 4-bromomethyl-benzoic methyl ester. NMR(CDCl<sub>3</sub>) 7.75-7.90 (m, 1H); 7.75-7.85 (m, 2H); 7.40-7.50 (m, 2H); 7.20-7.40 (m, 5H); 7.18 (s, 1H); 6.88-6.95 (m, 2H); 6.70-6.80 (m, 1H); 5.85-5.95 (m, 1H); 4.58-4.70 (m, 1H); 3.80 (s, 3H); 3.65 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H). (ESI/NH<sub>3</sub>)/MS: 530(M+H)<sup>+</sup>.

**Example 1271B**

16360 *N*-[4-*N*-(*N*-(3,5-difluorobenzyl)-*N*-(4-*N*-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dimethyl ester.

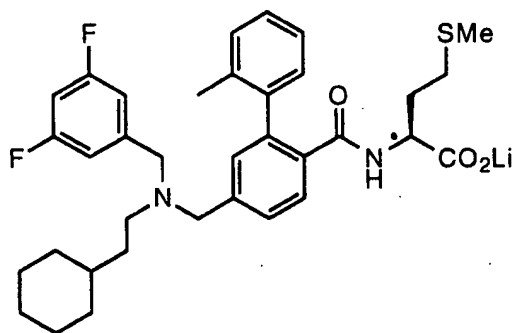
Prepared according to the procedure of example 1258C from 1271A. NMR(CDCl<sub>3</sub>) 7.75-7.90 (m, 1H); 7.75-7.85 (m, 2H); 7.40-7.50 (m, 2H); 7.20-7.40 (m, 5H); 7.18 (s, 1H); 6.88-6.95 (m, 3H); 6.70-6.80 (m, 1H); 5.85-5.95 (m, 1H); 4.90-4.95 (m, 1H); 4.58-4.70 (m, 1H); 3.80 (s, 3H); 3.65 (s, 3H); 3.60 (s, 2H); 3.55 (s, 2H); 2.58-2.70 (m, 2H); 2.0-2.15 (m, 10H); 1.7-2.0 (m, 3H); 1.5-1.7 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 792(M+H)<sup>+</sup>.



Example 1271C

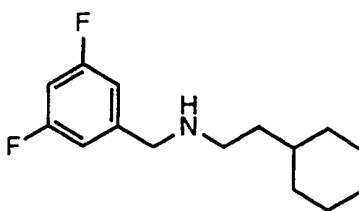
16370 *N*-[4-*N*-(*N*-(3,5-difluorobenzyl)-*N*-(4-*N*-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine dilithium salt.

Prepared according to the procedure of example 1178J from 1271B. NMR <sup>1</sup>H (d<sub>4</sub>-MeOH): 7.8-7.9 (2H, m); 7.6-7.7 (1H, m); 7.45-7.55 (4H, m); 7.1-7.3 (6H, m); 6.9-7.05 (2H, m); 6.75-6.85 (1H, m); 4.5-4.6 (1H, m); 4.2-4.3 (1H, m); 3.4-3.5 (6H, m); 2.5-2.6 (2H, m); 1.5-2.3 (15H, m). ESI(-)/MS: 762 (M-Li); 764(M+H); 781(M+NH<sub>4</sub>).



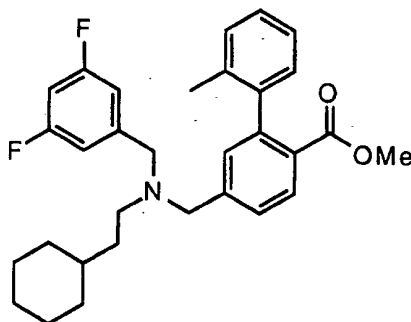
Example 1272

16380 *N*-[4-*N*-(*N*-(2-cyclohexylethyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Example 1272A

16385

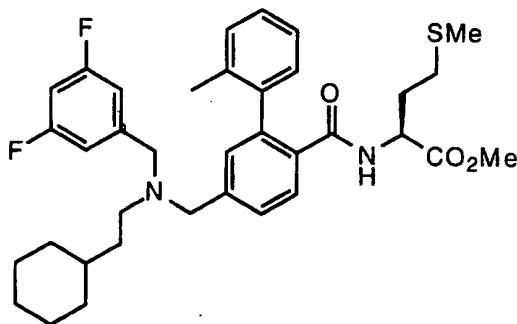
Prepared according to the procedure of example 1258A from reaction between 3,5-difluorobenzaldehyde and 2-cyclohexyle-1-aminoethane. NMR(CDCl<sub>3</sub>) 6.78-6.95 (m, 2H); 6.65-6.80 (m, 3H); 3.78 (s, 2H); 2.58-2.68 (m, 2H); 1.00-1.75 (m, 11H); 0.8-1.0- (m, 2H). (ESI/NH<sub>3</sub>)/MS: 254(M+H)<sup>+</sup>; 271(M+NH<sub>4</sub>)<sup>+</sup>.



16390

Example 1272B

Prepared according to the procedure of example 1226A from the reaction between 1272A and 4-Bromomethyl-2-(2-methylphenyl)benzoic acid, methyl ester. NMR(CDCl<sub>3</sub>) 7.91-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.10-7.30 (m, 4H); 7.05-7.15 (m, 1H); 6.83-6.95 (m, 2H); 6.60-6.78 (m, 1H); 3.60 (s, 5H); 3.55 (s, 2H); 2.40-2.50 (m, 2H); 2.05 (s, 3H); 1.50-1.75 (m, 5H); 1.30-1.47 (m, 2H); 1.00-1.38 (m, 4H); 0.74-0.90 (m, 2H). (ESI/NH<sub>3</sub>)/MS: 492(M+H)<sup>+</sup>.

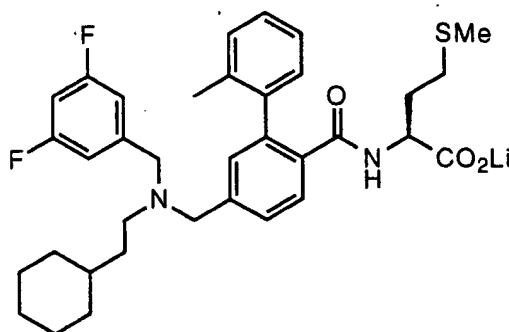


16400

Example 1272C

N-[4-N-(N-(2-cyclohexylethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

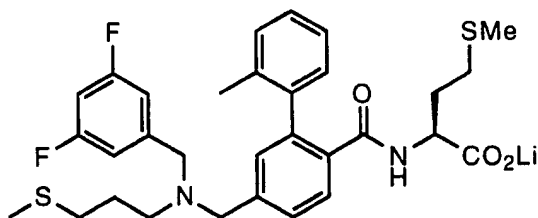
Prepared according to the procedure of example 1258C from 1272B. NMR(CDCl<sub>3</sub>)  
 7.81-7.98 (m, 1H); 7.38-7.45 (m, 2H); 7.20-7.40 (m, 3H); 7.18 (s, 1H); 6.83-6.95 (m,  
 2H); 6.60-6.78 (m, 1H); 5.81-5.90 (m, 1H); 4.58-4.70 (m, 1H); 3.67 (s, 3H); 3.60 (s,  
 2H); 3.55 (s, 2H); 2.40-2.50 (m, 2H); 2.00-2.20 (m, 8H); 1.70-2.00 (m, 1H); 1.50-1.70  
 (m, 5H); 1.30-1.50 (m, 2H); 1.10-1.38 (m, 4H); 0.74-0.90 (m, 2H). (ESI/NH<sub>3</sub>)/MS:  
 623(M+H)+.



#### Example 1272D

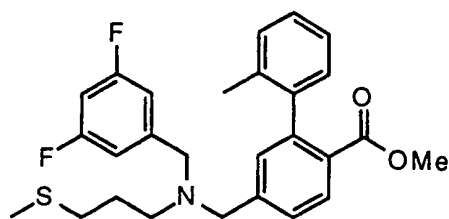
N-[4-N-(N-(2-cyclohexylethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1272C. NMR  
<sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m);  
 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 3.65 (2H, s); 3.58 (2H, s); 2.4-2.5 (2H, m); 2.21  
 (1H, m); 1.1-2.1 (20H, m); 0.8-0.9 (2H, m). ESI(-)/MS: 607(M-Li).

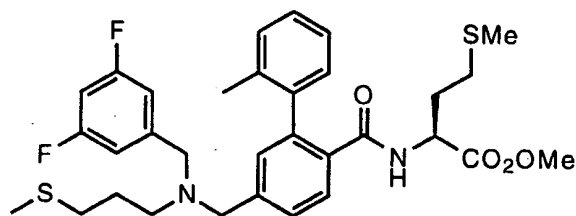


#### Example 1273

N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

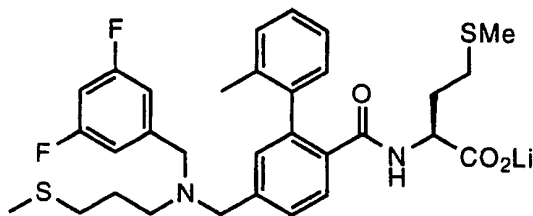
Example 1273A

Prepared according to the procedure of example 1258A from reaction between 1258A and 3-(methylthio)propionaldehyde. NMR(CDCl<sub>3</sub>) 7.91-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.20-7.30 (m, 4H); 7.04-7.10 (m, 1H); 6.83-6.90 (m, 2H); 6.60-6.74 (m, 1H); 3.60 (s, 5H); 3.55 (s, 2H); 2.50-2.60 (t, 2H); 2.42-2.50 (t, 2H); 2.10 (s, 3H); 2.05 (s, 3H); 1.70-1.84 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 470(M+H)<sup>+</sup>.

Example 1273B

N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

Prepared according to the procedure of example 1258C from 1273A. NMR(CDCl<sub>3</sub>) 7.81-7.98 (m, 1H); 7.38-7.45 (m, 2H); 7.20-7.40 (m, 3H); 7.18 (s, 1H); 6.83-6.95 (m, 2H); 6.60-6.78 (m, 1H); 5.81-5.90 (m, 1H); 4.58-4.70 (m, 1H); 3.67 (s, 3H); 3.63 (s, 2H); 3.55 (s, 2H); 2.50-2.60 (t, 2H); 2.42-2.50 (t, 2H); 1.92-2.20 (m, 9H); 1.65-1.95 (m, 4H); 1.5-1.65 (m, 2H). (DSI/NH<sub>3</sub>)/MS: 601(M+H)<sup>+</sup>.

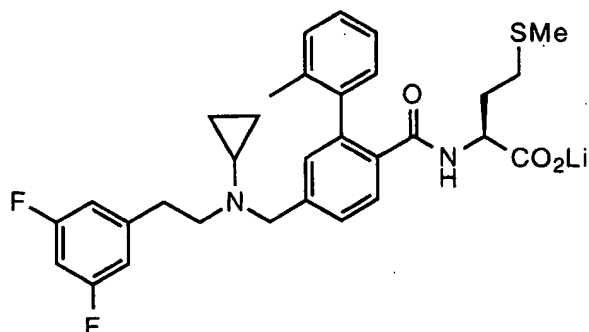
Example 1273C

N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

Prepared according to the procedure of example 1178J from 1273B. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.4-7.48 (1H, m); 7.0-7.3 (6H, m); 6.9-7.0 (2H, m);

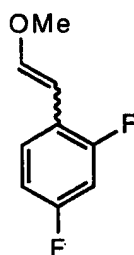


16450 6.7-6.8 (1H, m); 4.1-4.22 (1H, m); 4.65 (2H, s), 4.60 (2H, s); 2.5-2.6 (2H, m); 2.4-2.5 (2H, m); 1.8-2.3 (13H, m). ESI(-)/MS: 585(M-Li).



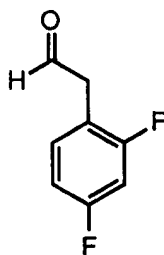
Example 1275

16455 N-[4-N-(N-cyclopropyl-N-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



Example 1275A

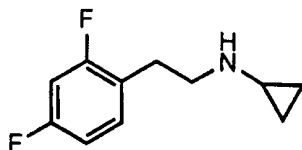
16460 Prepared according to the procedure of example 1279A from the reaction between 2,4-difluorobenzaldehyde and (Methoxymethyl)triphenylphosphonium chloride. NMR. 7.18-7.21 (m, 2H); 6.80-6.94 (m, 3H); 6.06 (s, 1H); 5.84 (s, 1H); 3.78 (s, 3H). DSI/NH<sub>3</sub>MS: 171(M+H)<sup>+</sup>; 188(M+NH<sub>4</sub>)<sup>+</sup>.



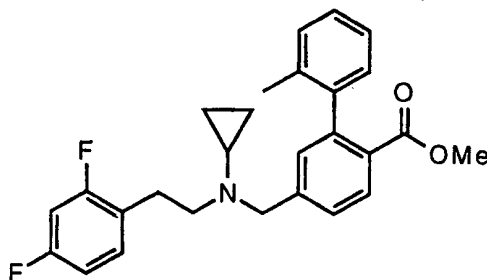
Example 1275B

16465 Prepared according to the procedure of example 1279B from example 1275A. NMR. 9.78 (s, 1H); 7.18-7.21 (m, 2H) 6.60-6.70 (m, 2H); ; 3.75 (s, 2H). DSI/NH<sub>3</sub>MS: 157(M+H)<sup>+</sup>; 174(M+NH<sub>4</sub>)<sup>+</sup>.

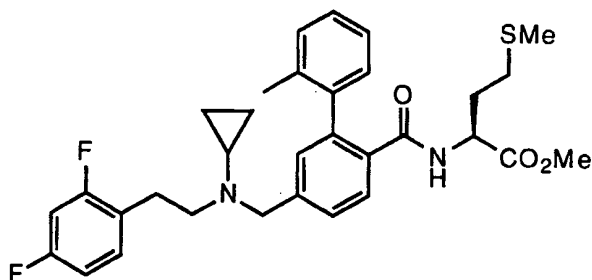
16470

Example 1275C

Prepared according to the procedure of example 1258A from the reaction between example 1275B and cyclopropylamine. NMR(CDCl<sub>3</sub>) 7.18-7.21 (m, 1H); 6.74-6.82 (m, 2H); 2.80-2.90 (m, 2H); 2.80-2.90 (m, 2H); 1.80-1.98 (m, 1H); 0.40-0.60 (m, 4H); (DSI/NH<sub>3</sub>)MS: 198(M+H)<sup>+</sup>.

Example 1275D

Prepared according to the procedure of example of 1258A from the reaction between example 1275C and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR 7.94-8.00 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 3.83 (s, 2H); 3.60 (s, 3H); 2.70-2.90 (m, 4H); 2.05 (s, 3H); 1.80-2.00 (m, 1H); 0.40-0.60 (m, 4H); (DSI/NH<sub>3</sub>)MS: 436(M+H)<sup>+</sup>.

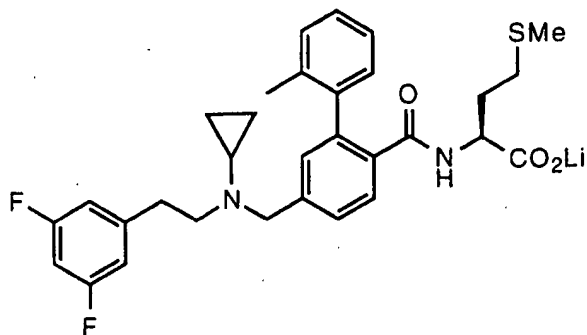


16485

Example 1275E

N-[4-N-(N-cyclopropyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

Prepared according to the procedure of example 1258C from 1275D. NMR 7.94-7.80 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 5.90-5.94 (m, 1H); 4.60-4.70 (m, 1H); 3.83 (s, 2H); 3.75 (s, 3H); 2.80-3.00 (m, 2H); 2.00-2.00 (m, 8H); 1.80-2.00 (m, 2H); 1.50-1.70 (m, 2H); 0.40-0.60 (m, 4H); (DSI/NH<sub>3</sub>)MS: 567(M+H)<sup>+</sup>.



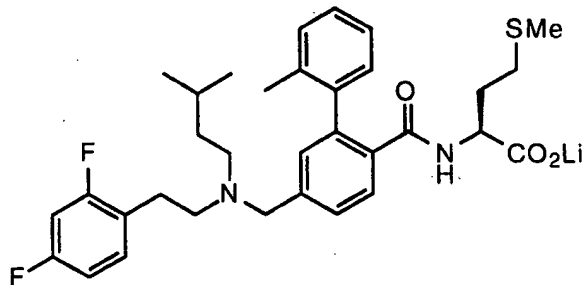
16495

Example 1275F

N-[4-N-(N-cyclopropyl-N-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

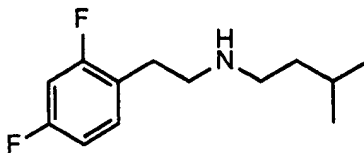
Prepared according to the procedure of example 1178J from 1275E. NMR  
 16500  $^1\text{H}$ (MeOH- $d_4$ ): 7.5-7.6 (1H, m); 7.25-7.35 (1H, m); 7.0-7.25 (7H, m); 6.7-6.8 (2H, m);  
 4.1-4.25 (1H, m); 3.8 (2H, s); 2.65-2.85 (4H, m); 1.65-2.2 (11H, m); 1.5-1.65 (1H, m);  
 0.4-0.5 (2H, m); 0.3-0.4 (2H, m). ESI(-)/MS: 551(M-Li). Anal. Calcd for  
 C<sub>31</sub>H<sub>33</sub>N<sub>2</sub>O<sub>3</sub>SLi•0.32H<sub>2</sub>O•1.0LiOH: C, 63.29; H, 5.93; N, 4.76. Found: C, 63.30; H,  
 5.77; N, 4.67.

16505

Example 1276

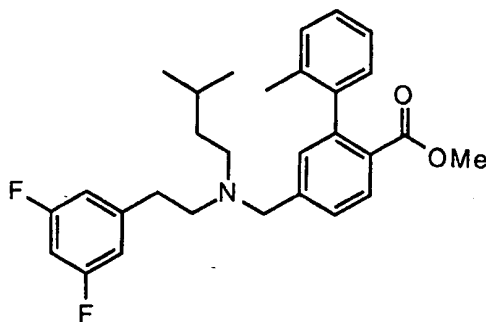
[4-N-(N-2-methylbutyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16510

Example 1276A

Prepared according to the procedure of example 1275C from example 1275B and 3-  
 16515 methylbutylamine. NMR(CDCl<sub>3</sub>) 7.14-7.22 (m, 1H); 6.74-6.82 (m, 2H); 2.78-2.90 (m,

4H); 2.60-2.68 (m, 2H); 1.50-1.70 (m, 1H); 1.30-1.50 (m, 2H); 0.9 (d, 6H).  
(DSI/NH<sub>3</sub>)MS: 228(M+H)<sup>+</sup>.

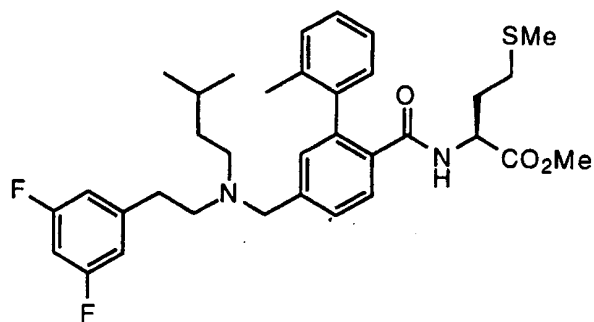


16520

Example 1276B

Prepared according to the procedure of example of 1258A from the reaction between example 1276A and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR 7.94-8.00 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 3.83 (s, 2H); 3.60 (s, 3H); 2.60-2.90 (m, 4H); 2.50-2.60 (m, 2H); 2.05 (s, 3H); 1.40-1.60 (m, 1H); 1.24-1.48 (m, 2H); 0.90 (d, 6H). (DSI/NH<sub>3</sub>)MS: 466(M+H)<sup>+</sup>.

16525

Example 1276C

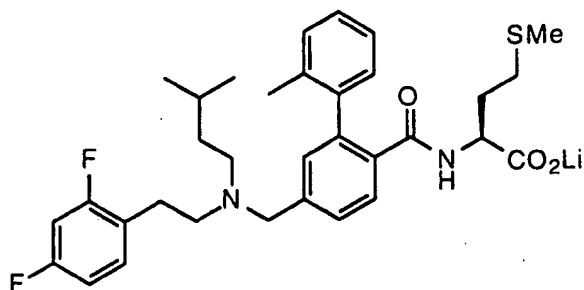
[4-N-(N-2-methylbutyl)-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

16530

Prepared according to the procedure of example 1258C from 1276B. NMR 7.85-7.95 (m, 1H); 7.00-7.40 (m, 7H); 6.67-6.82 (m, 2H); 5.91-5.97 (m, 1H); 4.56-4.70 (m, 1H); 3.63 (s, 5H); 2.65-2.80 (m, 4H); 2.46-2.55 (m, 2H); 2.00-2.20 (m, 8H); 1.70-2.00 (m, 1H); 1.45-1.70 (m, 2H); 1.30-1.40 (m, 2H); 0.90 (d, 6H). (DSI/NH<sub>3</sub>)MS:

16535

597(M+H)<sup>+</sup>.

**Example 1276D**

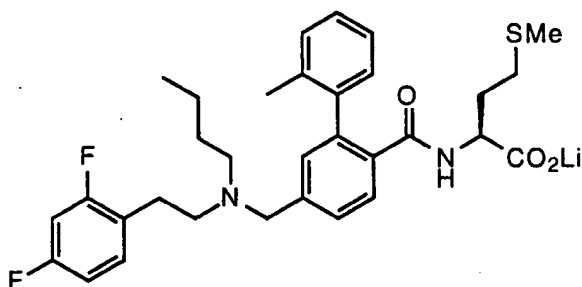
[4-N-(N-2-methylbutyl)-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16540

Prepared according to the procedure of example 1178J from 1276C. NMR

<sup>1</sup>H(MeOH-d<sub>4</sub>): 7.5-7.6 (1H, m); 7.2-7.3 (1H, m); 7.0-7.25 (7H, m); 6.7-6.8 (2H, m); 4.1-4.25 (1H, m); 3.8 (2H, s); 2.65-2.75 (2H, m); 2.55-2.65 (2H, m); 2.4-2.5 (2H, m); 2.1 (1H, s); 1.85-2.0 (6H, m); 1.55-1.85 (2H, m); 1.5-1.65 (1H, m); 1.38-1.5 (1H, m); 1.2-1.38 (2H, m); 0.75 (6H, d). ESI(-)/MS: 581(M-Li). Anal. Calcd for C<sub>33</sub>H<sub>39</sub>N<sub>2</sub>O<sub>3</sub>SLi•0.25H<sub>2</sub>O•1.8LiOH: C, 63.30; H, 5.54; N, 4.40. Found: C, 63.30; H, 6.17; N, 4.24.

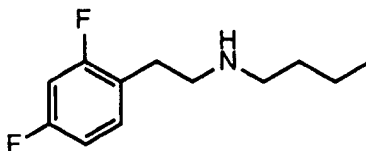
16545



16550

**Example 1277**

[4-N-(N-butyl)-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine lithium salt.

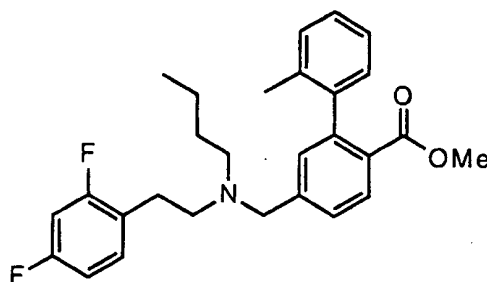


16555

**Example 1277A**

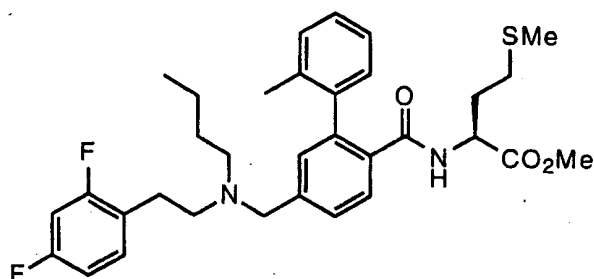
Prepared according to the procedure of example 1275C from example 1275B and butylamine. NMR(CDCl<sub>3</sub>) 7.14-7.22 (m, 1H); 6.74-6.82 (m, 2H); 2.78-2.90 (m, 4H);

16560 2.60-2.68 (m, 2H); 1.50-1.70 (m, 2H); 1.20-1.50 (m, 2H); 0.9 (d, 3H). (DSI/NH<sub>3</sub>)MS: 214(M+H)<sup>+</sup>.



#### Example 1277B

16565 Prepared according to the procedure of example of 1258A from the reaction between example 1277A and 4-formyl-2-(2-methylphenyl)benzoic acid methyl ester. NMR 7.94-8.00 (m, 1H); 7.00-7.40 (m, 7H); 6.74-6.82 (m, 2H); 3.83 (s, 2H); 3.60 (s, 3H); 2.60-2.90 (m, 4H); 2.50-2.60 (m, 2H); 2.05 (s, 3H); 1.40-1.60 (m, 2H); 1.24-1.48 (m, 2H); 0.90 t, 3H). (DSI/NH<sub>3</sub>)MS: 452(M+H)<sup>+</sup>.

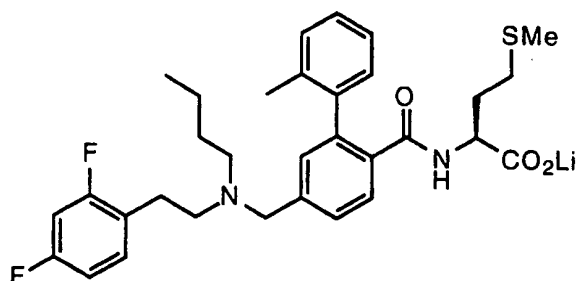


16570

#### Example 1277C

[4-N-(N-butyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

16575 Prepared according to the procedure of example 1258C from 1277B. NMR 7.85-7.95 (m, 1H); 7.00-7.40 (m, 7H); 6.67-6.82 (m, 2H); 5.91-5.97 (m, 1H); 4.56-4.70 (m, 1H); 3.63 (s, 5H); 2.65-2.80 (m, 4H); 2.46-2.55 (m, 2H); 2.00-2.20 (m, 8H); 1.70-2.00 (m, 2H); 1.45-1.70 (m, 2H); 1.30-1.40 (m, 2H); 0.90 (t, 3H). (DSI/NH<sub>3</sub>)MS: 583(M+H)<sup>+</sup>.



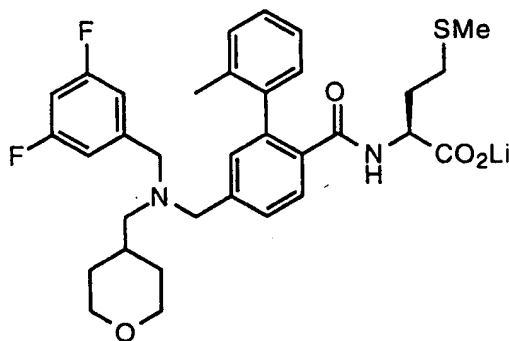
16580

Example 1277D

[4-*N*-(*N*-butyl-*N*-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

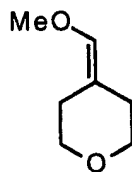
Prepared according to the procedure of example 1178J from 1277C. NMR  $^1\text{H}$ (MeOH- $d_4$ ): 7.45-7.55 (1H, m); 7.2-7.5 (1H, m); 7.0-7.25 (7H, m); 6.65-6.75 (2H, m); 4.1-4.25 (1H, m); 3.8 (2H, s); 2.65-2.75 (2H, m); 2.55-2.65 (2H, m); 2.35-2.45 (2H, m); 2.1 (1H, s); 1.8-2.0 (6H, m); 1.65-1.85 (2H, m); 1.4-1.6 (1H, m); 1.25-1.5 (3H, m); 1.1-1.25 (2H, m); 0.75 (3H, t). ESI(-)/MS: 567(M-Li). Anal. Calcd for  $\text{C}_{33}\text{H}_{39}\text{N}_2\text{O}_3\text{SLi} \cdot 1.7\text{H}_2\text{O}$ : C, 63.50; H, 6.73; N, 4.63. Found: C, 63.50; H, 6.41; N, 4.29.

16590

Example 1279

*N*-[4-*N*-(*N*-(4-methyltetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16595

Example 1279A

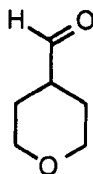
(Methoxymethyl)triphenylphosphonium chloride (25.71 g, 75 mmol) in 200 ml of anhydrous THF was treated 1.0 M sodium bis(trimethylsilyl)amide solution (75 ml, 75 mmol) at 0°C in 10 min. under  $\text{N}_2$ . The resulted deep red solution was then stirred at 0°C for another 1 hour. To this solution, tetrahydro-4-*H*-pyran-4-one (5.0 g, 50 mmol) in 10 ml of anhydrous THF was added. After being stirred at 0°C for another 1 hour, the solution was brought up to boiling for 12 hours. The reaction mixture was concentrated under vacuum, then diluted by 1:1 ether/hexane solution, filtrated through a pack of silica gel, and washed by another 200 ml of 1:1 ether/hexane solution. The filtrate was then concentrated. Vacuum distillation of the residue afforded 3.91 g of the title compound (64%).

16600

16605

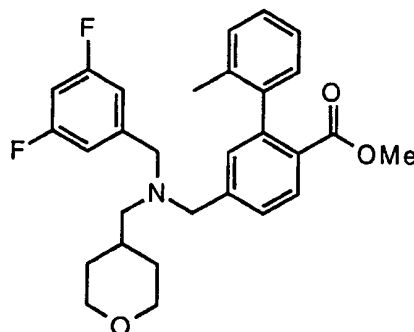
NMR(CDCl<sub>3</sub>) 5.83 (s, 1H); 3.4-3.5 (m, 4H); 3.58 (s, 3H); 2.29-2.35 (m, 2H); 2.05-2.15 (m, 2H). DSI/NH<sub>3</sub>/MS: 129(M+H)<sup>+</sup>; 146(M+NH<sub>4</sub>)<sup>+</sup>.

16610

Example 1279B

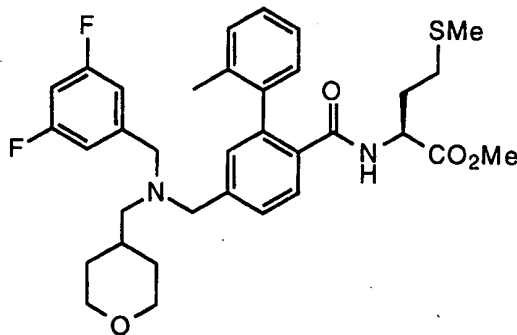
1279A (0.9 g, 7 mmol) in 15 ml of 88% formic acid plus 5 ml of water was refluxed for 3 hours under N<sub>2</sub>. After the solvents were removed by rotavapor, the residue was purified by flash chromatography eluting 3:7 EtOAc/hexane to afford 0.60 g of title compound (75%). NMR(CDCl<sub>3</sub>) 9.62 (s, 1H); 3.85-3.92 (m, 2H); 3.30-3.40 (m, 2H); 1.60-1.85 (m, 3H); 1.05-1.20 (m, 2H). DSI/NH<sub>3</sub>/MS: 115(M+H)<sup>+</sup>; 132(M+NH<sub>4</sub>)<sup>+</sup>.

16615

Example 1279C

Prepared according to the procedure of example 1258A from reaction between 1258A and 1279B. NMR(CDCl<sub>3</sub>) 7.92-7.99 (m, 1H); 7.35-7.45 (m, 1H); 7.20-7.30 (m, 4H); 7.05-7.10 (m, 1H); 6.82-6.90 (m, 2H); 6.62-6.73 (m, 1H); 3.88-3.98 (m, 2H); 3.61 (s, 3H); 3.59 (s, 2H); 3.52 (s, 2H); 3.25-3.40 (m, 2H); 2.25-2.31 (m, 2H); 2.05 (s, 3H); 1.60-1.90 (m, 3H); 1.00-1.20 (m, 2H). DSI/NH<sub>3</sub>/MS: 480(M+H)<sup>+</sup>.

16625

Example 1279D

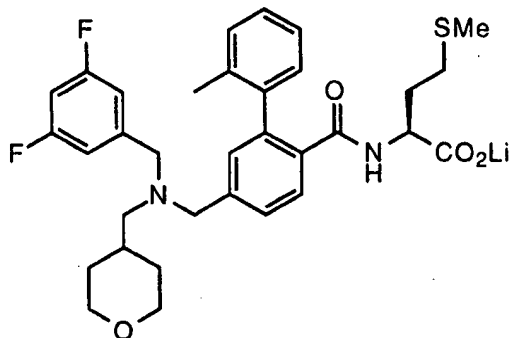


*N*-[4-*N*-(*N*-(4-methyltetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16630

Prepared according to the procedure of example 1258C from 1279C. NMR(CDCI<sub>3</sub>) 7.88-7.99 (m, 1H); 7.35-7.45 (m, 1H); 7.18-7.30 (m, 5H); 6.80-6.90 (m, 2H); 6.62-6.73 (m, 1H); 5.85-5.92 (m, 1H); 4.52-4.70 (m, 1H); 3.88-3.98 (m, 2H); 3.61 (s, 3H); 3.60 (s, 2H); 3.50 (s, 2H); 3.30-3.40 (m, 2H); 2.20-2.31 (m, 2H); 2.0-2.2 (m, 9H); 1.78-1.98 (m, 2H); 1.55-1.78 (m, 3H); 1.00-1.20 (m, 2H). DSI/NH<sub>3</sub>/MS: 611(M+H)<sup>+</sup>.

16635



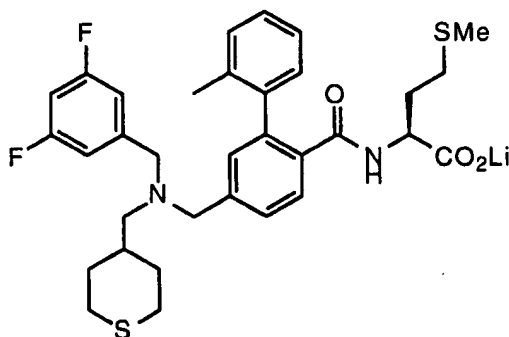
Example 1279E

*N*-[4-*N*-(*N*-(4-methyltetrahydropyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

16640

Prepared according to the procedure of example 1178J from 1279D. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.38-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.78-6.88 (1H, m); 4.1-4.22 (1H, m); 3.8-3.9 (2H, m); 3.8 (2H, s); 3.75 (2H, s); 3.4 (2H, m); 2.3-2.38 (2H, m); 2.25 (1H, s); 1.76-2.1 (14H, m); 1.0-1.2 (2H, m). ESI(-)/MS: 595(M-Li). Anal. Calcd for C<sub>33</sub>H<sub>37</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub>SLi•0.52H<sub>2</sub>O: C, 64.76; H, 6.26; N, 4.58. Found: C, 64.76; H, 6.01; N, 4.45.

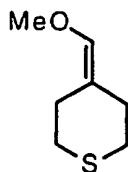
16645



16650

Example 1280

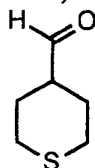
*N*-[4-*N*-(*N*-(4-methyltetrahydrothiopyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.



16655

Example 1280A

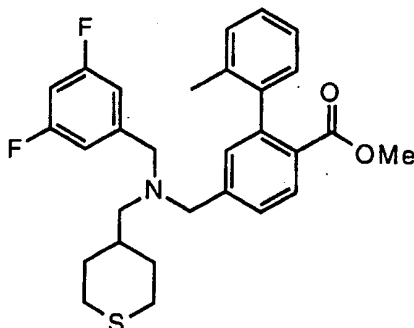
Prepared according to the procedure of example 1279A from tetrahydrothiopyran-4-one. NMR(CDCl<sub>3</sub>) 5.82 (s, 3H); 3.58 (s, 3H); 2.38-2.43 (m, 4H); 2.30-2.38 (m, 2H); 2.05-2.12 (m, 2H). DSI/NH<sub>3</sub>/MS: 145(M+H)<sup>+</sup>.



16660

Example 1280B

Prepared according to the procedure of example 1279B from 1280A. NMR(CDCl<sub>3</sub>) 9.65 (s, 1H); 2.60-2.80 (m, 4H); 2.20-2.40 (m, 2H); 1.70 1.88 (m, 2H). DSI/NH<sub>3</sub>/MS: 131(M+H)<sup>+</sup>.

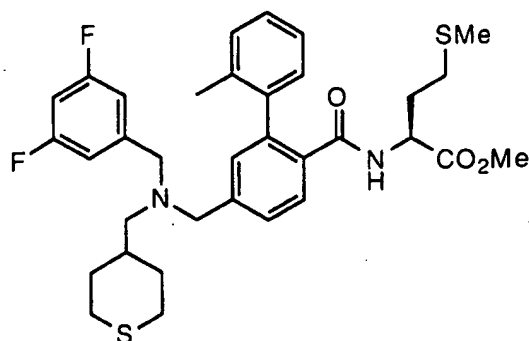


16665

Example 1280C

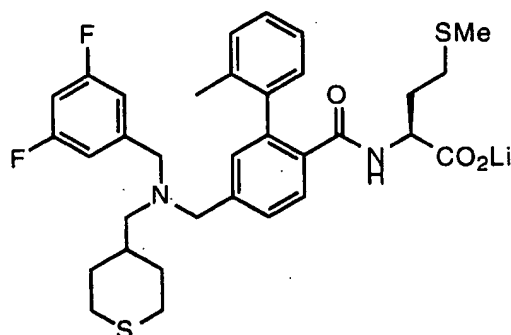
Prepared according to the procedure of example 1258A from reaction between 1258A and 1280B. NMR(CDCl<sub>3</sub>) 8.00-8.08 (m, 1H); 7.40-7.46 (m, 1H); 7.10-7.30 (m, 4H); 7.05-7.10 (m, 1H); 6.80-6.90 (m, 2H); 6.85-6.73 (m, 1H); 3.60 (s, 5H); 3.50 (s, 2H); 2.50-2.70 (m, 4H); 2.20-2.30 (m, 2H); 2.00-2.20 (m, 5H); 1.40-1.70 (m, 3H); 1.12-1.30 (m, 2H). DSI/NH<sub>3</sub>/MS: 496(M+H)<sup>+</sup>.

16670

**Example 1280D**

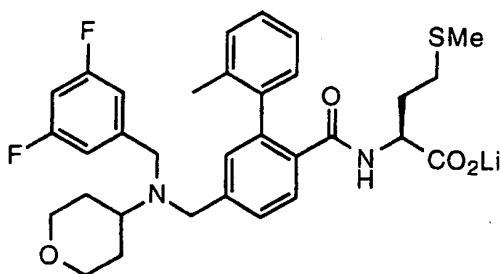
16675 *N*-[4-*N*-(*N*-(4-methyltetrahydrothiopyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester.

Prepared according to the procedure of example 1258C from 1280C. NMR(CDCl<sub>3</sub>) 7.85-8.00 (m, 1H); 7.1-7.45 (m, 6H); 6.80-6.90 (m, 2H); 6.65-6.76 (m, 1H); 5.84-5.94 (m, 1H); 4.55-4.70 (m, 1H); 3.65 (s, 3H); 3.52 (s, 2H); 3.45 (s, 2H); 2.50-2.70 (m, 4H);  
 16680 2.00-2.30 (m, 13H); 1.78-2.00 (m, 1H); 1.50-1.65 (m, 2H); 1.05-1.30 (m, 2H).  
 DSI/NH<sub>3</sub>/MS: 626(M+H)<sup>+</sup>.

**Example 1280E**

16685 *N*-[4-*N*-(*N*-(4-methyltetrahydrothiopyran-yl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

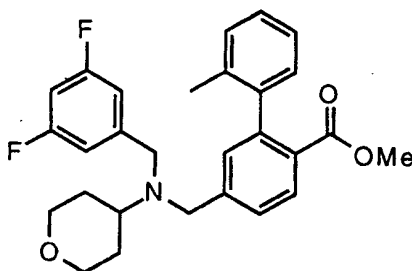
Prepared according to the procedure of example 1178J from example 1280D. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.6-7.7 (1H, m); 7.38-7.48 (1H, m), 7.0-7.35 (6H, m); 6.9-7.0 (2H, m); 6.75-6.85 (1H, m); 4.1-4.22 (1H, m); 3.6 (2H, s); 3.55(2H, s); 3.35 (2H, s); 2.4-2.65 (4H, m); 2.2-2.3 (3H, m); 1.78-2.1 (8H, m); 1.6-1.78 (2H, m); 1.05-1.2 (2H, m). ESI(-)/MS: 593(M-Li). Anal. Calcd for C<sub>33</sub>H<sub>37</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>Li•1.21H<sub>2</sub>O•1.0LiOH: C, 59.65; H, 6.13; N, 4.22. Found: C, 59.65; H, 5.85; N, 3.89.



16695

Example 1281

N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

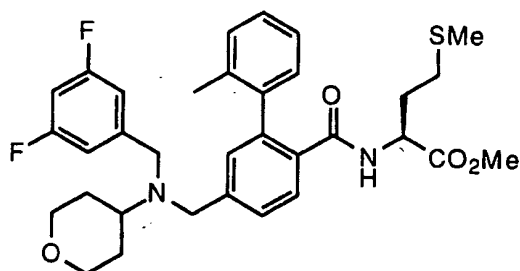


16700

Example 1281A

Prepared according to the procedure of example 1258A from reaction between 1258A and tetrahydro-4-H-pyran-4-one. NMR(CDCl<sub>3</sub>) 7.80-7.95 (m, 1H); 7.35-7.45 (m, 1H); 7.15-7.30 (m, 4H); 7.04-7.10 (m, 1H); 6.80-6.89 (m, 2H); 6.58-6.70 (m, 1H); 3.95-4.03 (m, 2H); 3.70 (s, 2H); 3.65 (s, 2H); 3.60 (s, 3H); 3.20-3.35 (m, 2H); 2.65-2.80 (m, 1H); 2.05 (s, 3H); 1.60-1.80 (m, 4H). (DSI/NH<sub>3</sub>)/MS: 466(M+H)<sup>+</sup>.

16705

Example 1281B

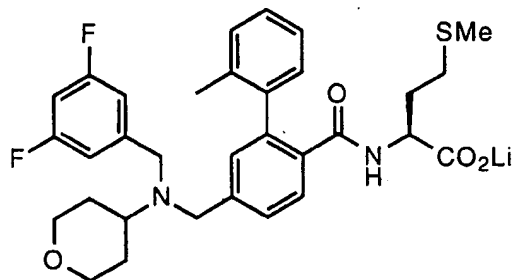
N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

16710

Prepared according to the procedure of example 1258C from 1281A. NMR(CDCl<sub>3</sub>) 7.81-7.98 (m, 1H); 7.38-7.45 (m, 1H); 7.20-7.40 (m, 4H); 7.18 (s, 1H); 6.83-6.91 (m, 2H); 6.60-6.70 (m, 1H); 5.81-5.90 (m, 1H); 4.58-4.70 (m, 1H); 3.95-4.02 (m, 2H); 3.70 (s, 2H); 3.63 (s, 2H); 3.60 (s, 2H); 3.20-3.38 (m, 1H); 2.55-2.80 (m, 1H); 1.92-2.20 (m,

16715

8H); 1.75-1.95 (m, 1H); 1.61-1.78 (m, 3H). 1.50-1.65 (m, 2H); (DSI/NH<sub>3</sub>)/MS: 597(M+H)<sup>+</sup>.



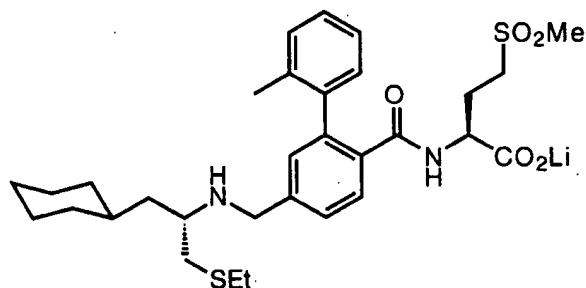
16720

Example 1281C

N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt.

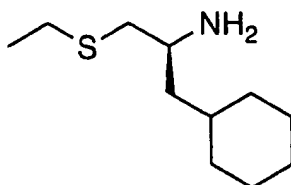
Prepared according to the procedure of example 1178J from 1281B. NMR <sup>1</sup>H(MeOH-d<sub>4</sub>): 7.58-7.68 (1H, m); 7.38-7.48 (1H, m), 7.0-7.28 (6H, m); 6.9-7.0 (2H, m); 6.78-6.88 (1H, m); 4.1-4.22 (1H, m); 3.9-4.0 (2H, m); 3.75 (2H, s); 3.7 (2H, s); 3.3 (2H, m); 2.7-2.85 (1H, m); 2.2 (1H, s); 1.76-2.1 (14H, m). ESI(-)/MS: 586(M-Li). Anal. Calcd for C<sub>32</sub>H<sub>35</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub>SLi•2.07H<sub>2</sub>O: C, 61.41; H, 6.30; N, 4.37. Found: C, 61.40; H, 6.05; N, 4.37.

16730

Example 1313

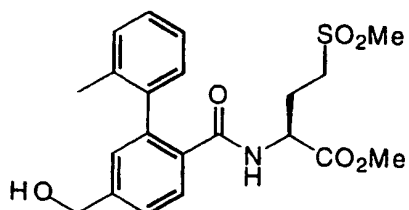
N-[4-(N-(3-Cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate Lithium Salt

16735

Example 1313A

2-Amino-3-cyclohexyl-1-ethylthioprop-2-ylamine

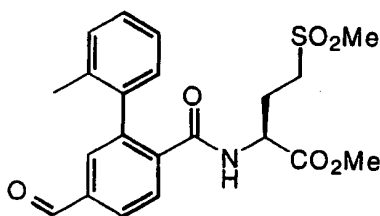
16740 Trifluoroacetic acid (3 mL) was added to a solution of the product from Example 403C (274 mg, 0.9 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) at ambient temperature. After 30 min of stirring, solvent was removed and the residue redissolved in CH<sub>2</sub>Cl<sub>2</sub>, washed with a solution of saturated K<sub>2</sub>CO<sub>3</sub>, dried (MgSO<sub>4</sub>) and concentrated. The crude product was chromatographed (silica gel; CHCl<sub>3</sub>/MeOH, 90:10) to afford a clear oil (162 mg, 75%): <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  2.97 (m, 1H), 2.68 (dd, J=13, 4 Hz, 1H), 2.55 (q, J=7.5 Hz, 2H), 2.34 (dd, J=13, 8.5 Hz, 1H), 1.80-1.61 (m, 5H), 1.50-1.10 (m, 6H), 1.26 (t, J=7.5 Hz, 3H), 1.00-0.90 (m, 2H); MS (CI/NH<sub>3</sub>) m/z: 202 (M+H)<sup>+</sup>.



16750 Example 1313B

Methyl-N-[4-(hydroxymethyl)-2-(2-methylphenyl)benzoyl]-2-amino-4-methylsulfonylbutanoate

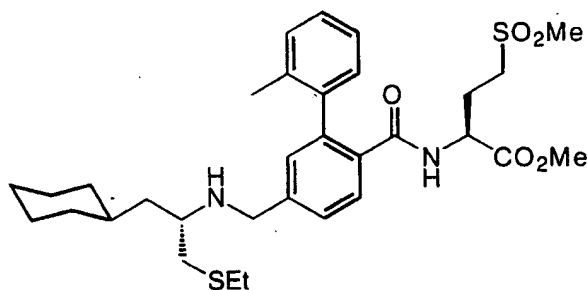
The product from Example 1178C (1.0 g, 4.1 mmol) in MeOH (12 mL) was combined with a solution of saturated LiOH (4.0 mL) and heated at reflux for 3.5 hours. The mixture was allowed to cool to ambient temperature and then extracted with Et<sub>2</sub>O. The phases were separated and concentrated HCl added to the aqueous phase which was extracted with EtOAc (2X). The EtOAc phases were combined, dried (MgSO<sub>4</sub>) and concentrated to dryness to afford the crude acid as a white solid. MS (CI/NH<sub>3</sub>) m/z: 243 (M+H)<sup>+</sup>. The crude acid, EDCI (940 mg, 4.5 mmol), Hobt (1.1 g, 8.2 mmol), (L)-methionine sulfone methyl ester hydrochloride (1.0 mg, 4.5 mmol) and DIEA (2.1 mL, 12.3 mmol) in DMF (15 mL) were allowed to react in a manner similar to that described in Example 608 D. The crude residue was chromatographed (silica gel; MeOH/CHCl<sub>3</sub>, 5:95) to afford the title compound (963 mg, 56%).



16765 Example 1313C

Methyl-N-[4-(formyl)-2-(2-methylphenyl)benzoyl]-2-amino-4-methylsulfonylbutanoate

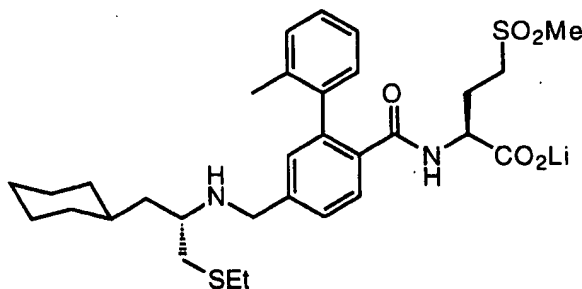
Dimethylsulfoxide (325  $\mu$ L, 4.6 mmol) was added to a solution of oxalyl chloride (200  $\mu$ L, 2.5 mmol) at  $-78^{\circ}\text{C}$ . After stirring for 5 min, the product from Example 1313B (955 mg, 2.3 mmol) in  $\text{CH}_2\text{Cl}_2$  (2.5 mL) was added to the reaction vessel. After 15 min, TEA (950  $\mu$ L, 6.8 mL) was added to the reaction mixture and the cold bath was removed. After stirring for 30 min, a solution of 2N HCl was added to the mixture and the phases separated. The organic phase was dried ( $\text{MgSO}_4$ ) and concentrated. The residue was chromatographed (silica gel;  $\text{MeOH}/\text{CHCl}_3$ , 2:98) to afford a clear oil (866 mg, 91%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.88 (m, 1H), 2.11-2.30 (m, 4H), 2.47-2.73 (m, 2H), 2.71 (s, 3H), 3.71 (s, 3H), 4.65 (m, 1H), 6.12 (dd,  $J=8.8$  Hz, 1H), 7.20 (d,  $J=7$  Hz, 1H), 7.27-7.41 (m, 2H), 7.76 (s, 1H), 7.95-8.06 (m, 2H), 10.10 (s, 1H); MS ( $\text{CI}/\text{NH}_3$ )  $m/z$ : 418 ( $\text{M}+\text{H}$ ) $^+$ .



Example 1313D

Methyl-N-[4-(N-(3-Cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate

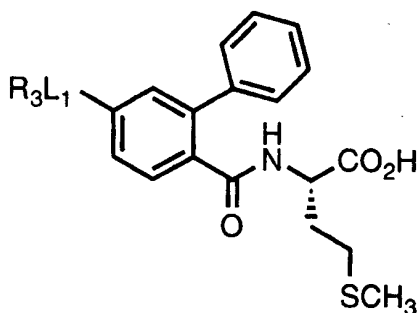
The product from Example 1313A (285 mg, 1.4 mmol), the product from Example 1313C (618 mg, 1.5 mmol) and sodium triacetoxyborohydride (415 mg, 2.0 mmol) were combined in 1,2-dichloroethane (6 mL) at ambient temperature and allowed to stir for 18 hours. A solution of saturated  $\text{NaHCO}_3$  was added and the mixture was extracted with  $\text{EtOAc}$  (2X). The  $\text{EtOAc}$  phases were combined, dried ( $\text{MgSO}_4$ ) and concentrated. The residue was chromatographed (silica gel;  $\text{MeOH}/\text{CHCl}_3$ , 2:98) to afford a clear oil (753 mg, 89%). MS ( $\text{CI}/\text{NH}_3$ )  $m/z$ : 418 ( $\text{M}+\text{H}$ ) $^+$ .



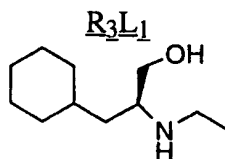
Example 1313E

N-[4-(N-(3-Cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate Lithium Salt

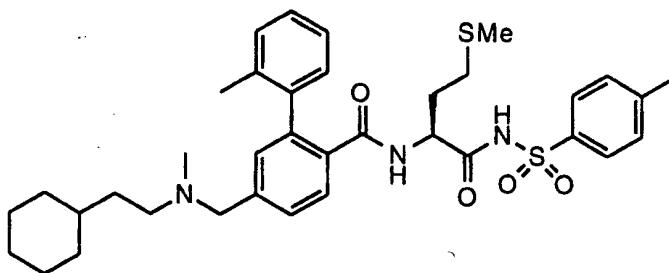
16795 The product from Example 1313D (748 mg, 1.2 mmol) was allowed to react with lithium hydroxide monohydrate (55 mg, 1.3 mmol) in a manner similar to that described in Example 608E to afford the title compound. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 300 MHz) δ 0.70-0.91 (m, 2H), 1.12-1.65 (m, 14H), 1.75-2.20 (m, 5H), 2.35-2.67 (m, 7H), 2.82 (s, 3H), 3.66-3.86 (m, 3H), 6.95 (m, 1H), 7.10-7.25 (m, 4H), 7.38 (d, J=8 Hz, 1H), 7.53 (d, J=8 Hz, 1H); MS (APCI(-)) m/z: (M-H)<sup>-</sup> 587; Anal. Calcd for C<sub>31</sub>H<sub>43</sub>LiN<sub>2</sub>O<sub>5</sub>S<sub>2</sub>•1.90 H<sub>2</sub>O: C, 59.20; H, 7.50; N, 4.45. Found: C, 59.22; H, 7.16; N, 4.36.



16805

Example 1317Example 1317

MS (M+H)<sup>±</sup>  
499



16810

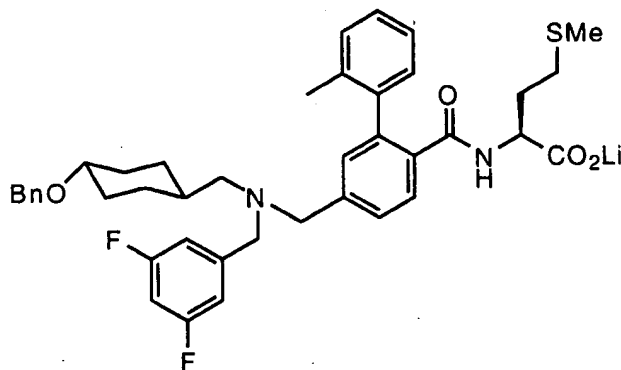
Example 1319

N-[4-(N-Methyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine p-tolylsulfonimide

The above compound was prepared from the compound described in Example 608E and p-toluenesulfonamide by the method of Example 1216A, except the reaction was



- 16815 worked up by diluting with  $\text{CHCl}_3$  (instead of EtOAc), there was no HCl wash, and the chromatography was done with EtOAc/water/ $\text{CH}_3\text{CO}_2\text{H}$  19/0.5/0.5, then 18/1/1.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.80 (m, 3H), 7.58 (dd, 1H), 7.22 (m, 7H), 6.18 (m, 1H), 4.20 (m, 1H), 3.98 (s, 2H), 2.80 (m, 2H), 2.55 (s, 3H), 2.40 (s, 3H), 2.00 (m, 8H), 1.60 (m, 8H), 1.40, 1.20, 0.90 (all m, total 7H). MS (ESI) 648 (M-H) $^-$ . Anal calcd for  $\text{C}_{36}\text{H}_{47}\text{N}_3\text{O}_4\text{S}_2 \cdot 1.00$
- 16820  $\text{H}_2\text{O}$ : C, 64.74; H, 7.39; N, 6.29. Found: C, 64.53; H, 7.22; N, 6.06.

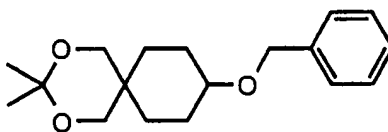
Example 1332

- 16825 *N*-[4-*N*-(*N*-(*trans*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

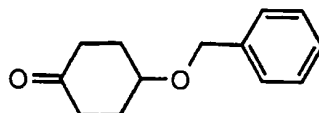
Example 1332A

- 16830 A mixture of 1,4-cyclohexanedione *mono*-2,2-dimethyltrimethylene ketal (1.98 g, 10 mmol), and sodium borohydride (0.757 g, 20 mmol) in 100 ml of methanol was stirred for 12 hours. The methanol was removed under reduced pressure. The residue was taken into ethyl acetate, washed by 10 % NaOH and brine respectively, and the dried over anhydrous MSG. Yield: 1.60 g (80%). (SDI/ $\text{NH}_3$ ) MS: 201(M+H) $^+$ ; 218(M+ $\text{NH}_4$ ) $^+$ .

16835

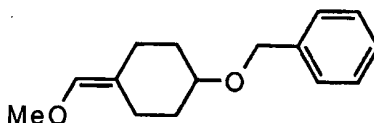
Example 1332B

Prepared according to the procedure of example 1252 from the reaction between example 1332A and benzyl bromide. NMR(CDCl<sub>3</sub>) 7.20-7.35 (m, 5H); 4.57 (s, 2H); 3.45-3.55 (m, 6H); 2.00-2.15 (m, 2H); 1.50-1.82 (m, 5H). (SDI/NH<sub>3</sub>) MS: 291(M+H)<sup>+</sup>; 308(M+NH<sub>4</sub>)<sup>+</sup>.



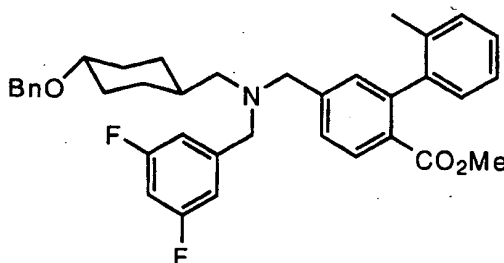
Example 1332C

Prepared according to the procedure of example of example 1266A from the reaction of example 1232B and HCl. NMR(CDCl<sub>3</sub>) 7.23-7.40 (m, 5H); 4.60 (s, 2H); 3.78-4.08 (m, 1H); 2.55-2.70 (m, 2H); 2.20-2.35 (m, 2H); 2.10-2.20 (m, 2H); 1.90-2.01 (m, 2H). (SDI/NH<sub>3</sub>) MS: 222(M+H)<sup>+</sup>; 239(M+NH<sub>4</sub>)<sup>+</sup>.



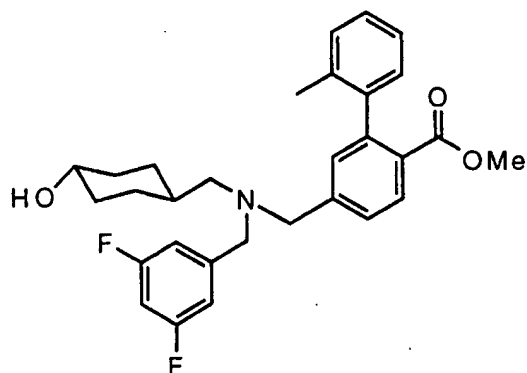
Example 1332D

Prepared according to the procedure of example 1279A from the reaction between example 1232C and (Methoxymethyl)triphenylphosphonium chloride. NMR(CDCl<sub>3</sub>) 7.23-7.40 (m, 5H); 5.85 (s, 1H); 4.60 (s, 2H); 3.63-3.75 (m, 5H); 2.58-2.70 (m, 1H); 2.10-2.30 (m, 1H); 1.4-2.0 (m, 5H). (SDI/NH<sub>3</sub>) MS: 233(M+H)<sup>+</sup>; 250(M+NH<sub>4</sub>)<sup>+</sup>.



Example 1332E

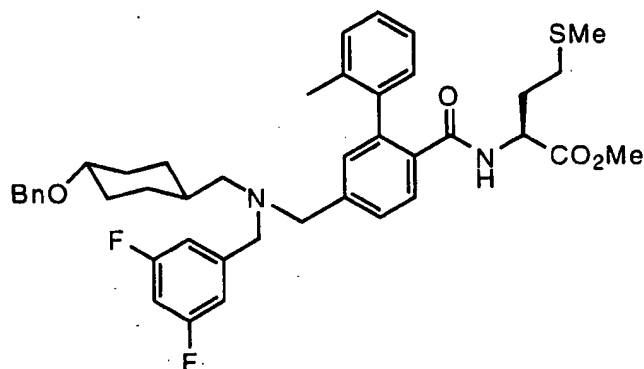
Example 1332D was hydrolyzed in formic acid according to the example 1279B to give corresponding aldehyde, which was used to react with example 1258A to give two isomers. One is example 1232E, the other is example 1233A. NMR(CDCl<sub>3</sub>) 7.90-7.95 (m, 1H); 7.38-7.44 (m, 1H); 7.13-7.39 (m, 9H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 4.55 (s, 2H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 4H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH<sub>3</sub>) MS: 584(M+H)<sup>+</sup>.

Example 1332F

16870 A mixture of 1332D (0.07 g, 0.12 mmol) and 0.1 ml of trimethylsilyl iodide in 2 ml of methylene chloride was stirred until TLC indicated that there was no starting material left. Flash chromatography of the residue afforded 0.042 g of the title compound (71%).

NMR(CDCl<sub>3</sub>) 7.90-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.39 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 4H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH<sub>3</sub>) MS: 494(M+H)<sup>+</sup>.

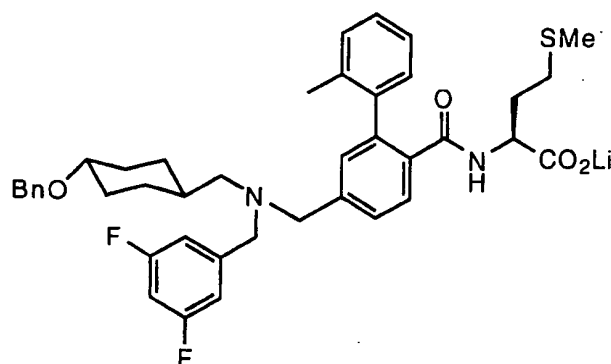
16875

Example 1332G

Prepared according to the procedure of example 1258C from example 1232F.

16880 NMR(CDCl<sub>3</sub>) 7.83-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 5.84-5.90 (m, 1H); 4.55-4.67 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 16H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH<sub>3</sub>) MS: 624(M+H)<sup>+</sup>.

16885

**Example 1332H**

*N*-[4-*N*-(*N*-(*trans*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

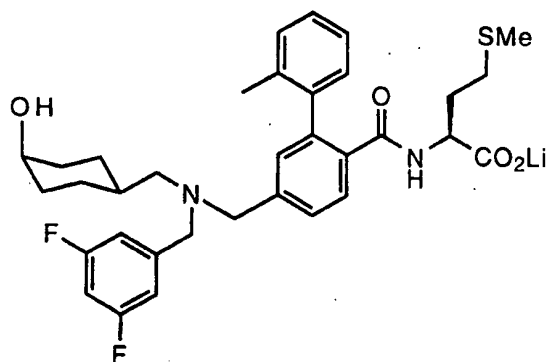
16890

Prepared according to the procedure of example 1178J from example 1332G.

NMR(CDCl<sub>3</sub>) 7.60-7.70 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 5H); 6.83-7.00 (m, 2H); 6.68-6.72 (m, 1H); 4.20-4.30 (m, 1H); 3.60 (m, 2H); 3.55 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 16H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). ESI(-)/MS: 609(M-Li). Anal. Calcd for C<sub>34</sub>H<sub>39</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub>SLi•2.00

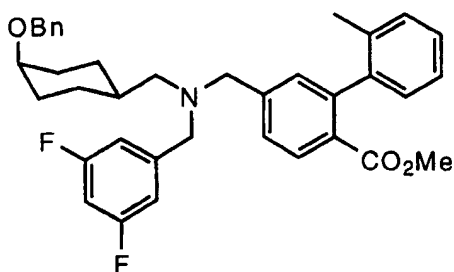
16895

LiOH: C, 61.45; H, 6.22; N, 4.22. Found: C, 61.56; H, 5.88; N, 3.94.

**Example 1333**

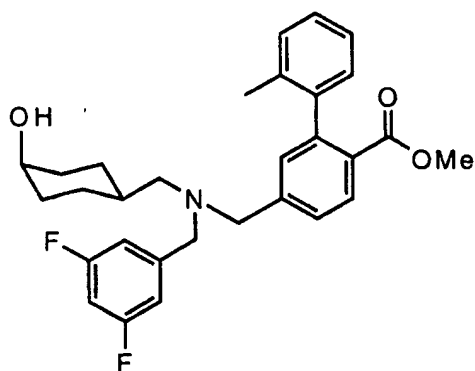
*N*-[4-*N*-(*N*-(*cis*-4-hydroxycyclohexyl)-*N*-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

16900

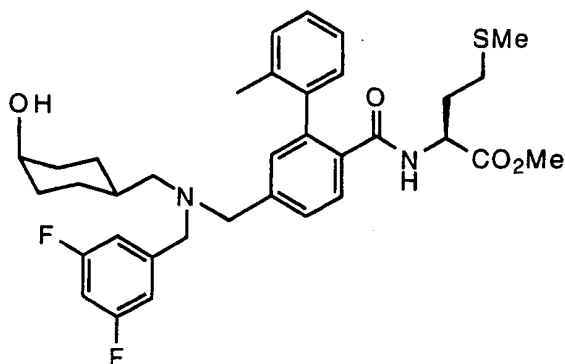
Example 1333A

16905 Prepared according to the procedure of example 1332E. NMR(CDCl<sub>3</sub>) 7.90-7.95 (m, 1H); 7.38-7.44 (m, 1H); 7.13-7.39 (m, 9H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 4.55 (s, 2H); 3.90-4.00 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 3H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH<sub>3</sub>) MS: 584(M+H)<sup>+</sup>.

16910

Example 1333B

16915 Prepared according to the procedure of example 1332F from the reaction between 1333B and trimethylsilyl iodide. NMR(CDCl<sub>3</sub>) 7.90-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.39 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 3.90-4.00 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 2.0-2.18 (m, 3H); 1.80-2.00 (m, 2H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH<sub>3</sub>) MS: 494(M+H)<sup>+</sup>.

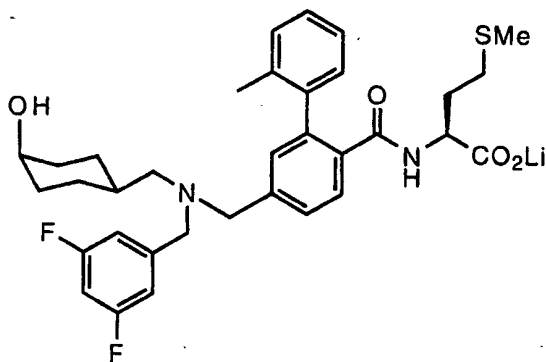


16920

Example 1333C

Prepared according to the procedure of example 1258C from example 1333B.

16925 NMR(CDCl<sub>3</sub>) 7.83-7.95 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 4H); 7.02-7.10 (m, 1H); 6.83-6.92 (m, 2H); 6.60-6.70 (m, 1H); 5.84-5.90 (m, 1H); 4.55-4.67 (m, 1H); 3.92-4.02 (m, 1H); 3.60 (s, 3H); 3.55 (m, 2H); 3.50 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 15H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). (SDI/NH<sub>3</sub>) MS: 624(M+H)<sup>+</sup>.



16930

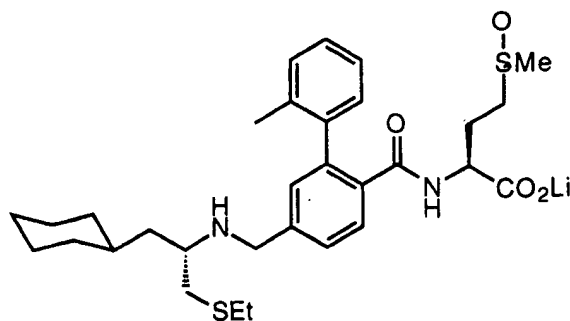
Example 1333D

N-[4-N-(N-(cis-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt

Prepared according to the procedure of example 1178J from example 1333C.

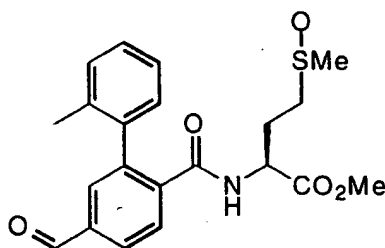
16935 NMR(CDCl<sub>3</sub>) 7.60-7.70 (m, 1H); 7.40-7.44 (m, 1H); 7.13-7.40 (m, 5H); 6.83-7.00 (m, 2H); 6.68-6.72 (m, 1H); 4.20-4.30 (m, 1H); 3.92-4.01 (m, 1H); 3.60 (m, 2H); 3.55 (m, 2H); 3.18-4.30 (m, 1H); 2.18-2.21 (m, 2H); 1.80-2.25 (m, 15H); 1.40-1.60 (m, 2H); 1.09-1.32 (m, 2H); 0.67-0.83 (m, 2H). ESI(-)/MS: 609(M-Li). Anal. Calcd for C<sub>34</sub>H<sub>39</sub>F<sub>2</sub>N<sub>2</sub>O<sub>4</sub>SLi•2.50 LiOH•0.57H<sub>2</sub>O: C, 62.58; H, 6.26; N, 4.29. Found: C, 61.61; H, 5.99 N, 3.92.

16940

Example 1334

(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate Lithium Salt

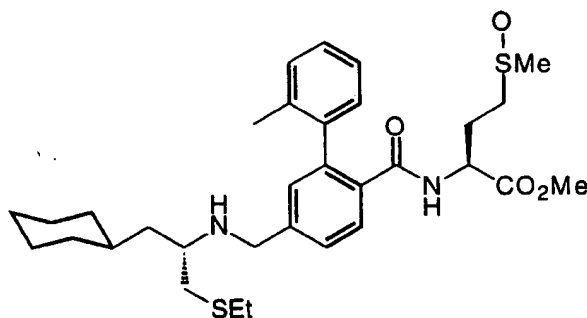
16945

Example 1334A

(2S) 2-N-[4-formyl-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, Methyl Ester

16950

The title compound was prepared from N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester (example 403G) according to the procedure in example 1071D, and was isolated as a light yellow oil. MS(APCI(+)) 402 (M+H)<sup>+</sup>. MS(APCI(-)) 436 (M+Cl)<sup>-</sup>, 400 (M-H)<sup>-</sup>.



16955

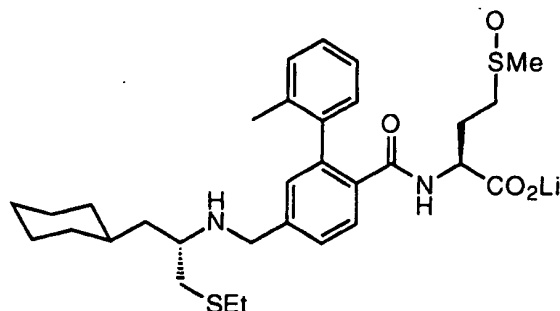
Example 1334B

(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, Methyl Ester

The title compound was prepared according to example 403H, substituting (2S) 2-N-[4-formyl-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate methyl ester for N-

16960

[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester. MS(APCI(+)) 587 (M+H)<sup>+</sup>. MS(APCI(-)) 621 (M+Cl)<sup>-</sup>.



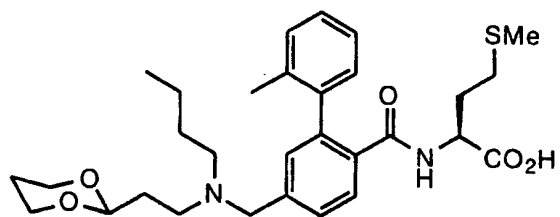
16965

### Example 1334C

(2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, Lithium Salt

The title compound was prepared from (2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate methyl ester according to the procedure in example 608E, with the exception that the product was isolated as a light yellow foam after concentrating a methanolic solution under reduced pressure. <sup>1</sup>H NMR (300 MHz, DMSO) δ 0.66-0.90 (m, 2H), 1.02-1.80 (m, 13H), 1.10 (t, J=7.2 Hz, 3H), 1.96-2.21 (m, 5H), 2.36 (s, 1.5H), 2.39 (s, 1.5H), 2.41 (q, J=7.2 Hz, 2H), 2.56-2.67 (m, 3H), 3.60-3.84 (m, 4H), 6.98 (brd, J=6 Hz, 1H), 7.08-7.23 (m, 5H), 7.38 (d, J=8.4 Hz, 1H), 7.49 (d, J=7.8 Hz, 0.5H), 7.51 (d, J=7.8 Hz, 0.5H). MS (APCI(-)) m/e 571 (M-H).

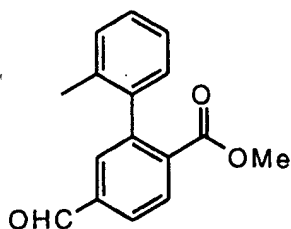
16980



### Example 1335

N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

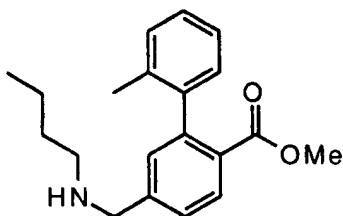




16985

Example 1335A4-Formyl-2-(2-methylphenyl)benzoic acid methyl ester

Following the procedure of example 1134D, example 1178 C (3.30 g, 11.82 mmol) provided 3.00 g 100%) of the title compound. MS (DCI, NH<sub>3</sub>): 255 (MH<sup>+</sup>).

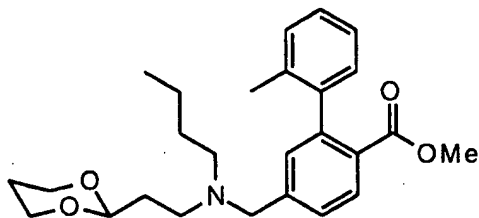


16990

Example 1335B4-(n-Butylaminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

Following the procedure of example 1106D, part 1 example 1335A (1.27 g, 5.00 mmol) and butyl amine (0.99 mL, 10.00 mmol) provided 1.45 g (94%) of the title compound. MS (DCI, NH<sub>3</sub>): 312 (MH<sup>+</sup>).

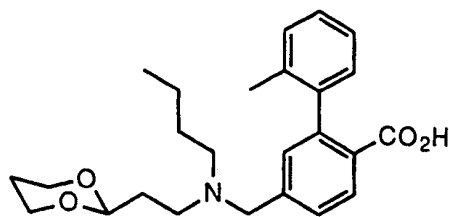
16995

Example 1335C4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

17000

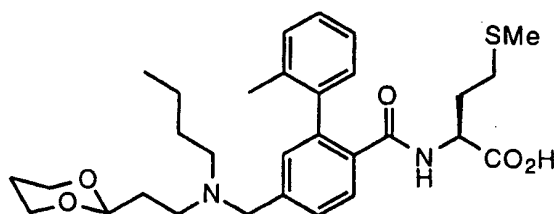
A solution of example 1335B (359 mg 1.15 mmol), 2-bromoethyl-1,3-dioxane (164 μL, 1.2 mmol), TBAI (443 mg, 1.2 mmol) and diisopropylethylamine (260 μL, 1.5 mmol) in 3 mL of DMF were heated to 60°C for 72 hours. The cooled reaction mixture was diluted with water and extracted with 3 portions of ethyl ether. The combined organic extracts were washed with water, brine, dried, filtered and concentrated. The residue was purified by column chromatography on silica gel (25 g, 25% ethyl acetate/hexanes) provided 330 mg (78%) of the title compound. MS: (ESI<sup>+</sup>) 426 (MH<sup>+</sup>).

17005

Example 1335D

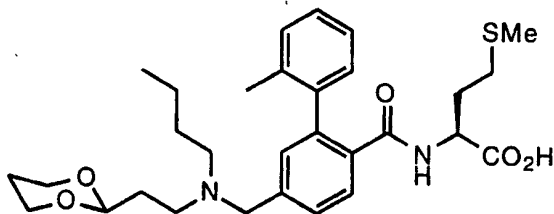
4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoic acid,

17010 Following the procedure of example 1130D, example 1335C (310 mg, 0.72 mmol) provided 222 mg (75%) of the title compound. MS (ESI+): 412 (MH+); (ESI-): 410 (M-H).

Example 1335E

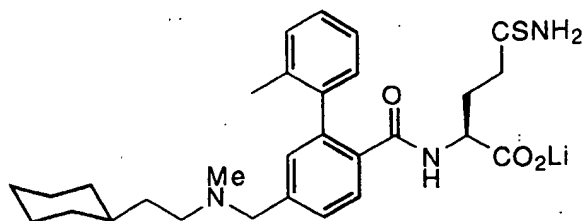
N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, methyl ester

17015 Following the procedure of example 1178I, example 1335D (85 mg, 0.25 mmol) provided 57 mg (50%) of the title compound. MS (ESI+): 557 (MH+); (ESI-): 555 (M-H).

Example 1335F

N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine

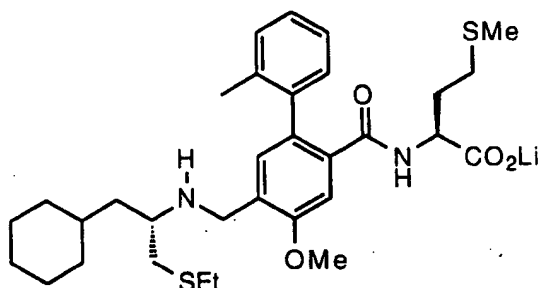
17025 Following the procedure of example 1104D, example 1335 E (55 mg (0.10 mmol) provided 30 mg of the title compound. <sup>1</sup>H nmr (300 MHz., CD<sub>3</sub>OD): δ 7.64, d, 1H; 7.49, dd, 1H; 7.29, m, 1H; 7.02 - 7.22, m, 4H; 4.64, t, 1H; 4.29, m, 3H; 3.91, ddd, 2H; 3.66, dt, 2H; 3.22, m, 2H; 3.03, m, 2H; envelope 1.74 - 2.16, m, 12H; 1.62, m, 3H; 1.18 - 1.36, mn, 3H; 0.88, t, 3H. MS (ESI+): 543 (MH+); (ESI-): 541 (M-H). Calc'd for C<sub>31</sub>H<sub>43</sub>N<sub>2</sub>O<sub>5</sub>S•1.30 H<sub>2</sub>O; C 63.64; H 7.94; N 4.95; Found: C 63.63; H 7.37; N 5.07.

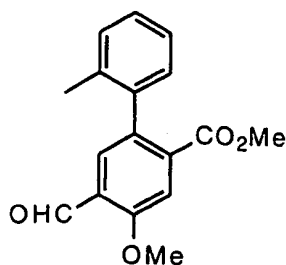
**Example 1336****N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thioglutamine Lithium Salt**

17035 *N*-[4-(*N*-(2-cyclohexylethyl)-*N*-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thioglutamine methyl ester (12 mg, 22.9  $\mu$ mol) was saponified using the standard LiOH procedure, evaporated, and lyophilized from water to provide 9.8 mg of the title compound. MS *m/e* 514 (*M*-H)<sup>-</sup>.

**Example 1336B****N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thioglutamine Methyl Ester**

17040 *N*-[4-(*N*-(2-cyclohexylethyl)-*N*-methylaminomethyl)-2-(2-methylphenyl)benzoyl]glutaminitrile methyl ester, see Example 1041, (139 mg, 0.28 mmol) was dissolved in 5 mL pyridine with TEA (0.5 mL). Excess H<sub>2</sub>S was bubbled into the solution which was then sealed and stirred at room temperature for 18 hours. The reaction was evaporated to dryness, dissolved in EtOAc, washed with water and brine, and chromatographed (50 % EtOAc/hexanes) to give 13 mg of the methyl ester. MS *m/e* 524 (*M*+H)<sup>+</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  0.82 (m, 2H), 1.11 (m, 3H), 1.32 (m, 5H), 1.6 (m, 7H), 2.18 (m, 6H), 2.32 (m, 1H), 2.58 (m, 1H), 2.75 (m, 1H), 3.53 (m, 2H), 3.72 (s, 3H), 6.9-7.5 (m, 9H), 7.83 (m, 1H).

**Example 1337****N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine**

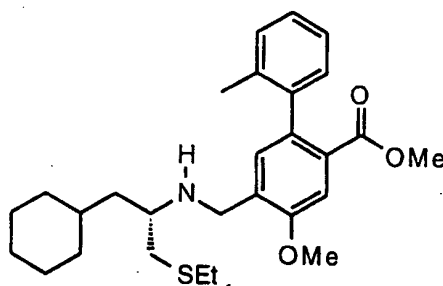


17060

Example 1337A2-(2-Methylphenyl)-4-formyl-5-methoxybenzoic acid, methyl ester

A solution of example 1134D (180 mg, 0.63 mmol) in 2 mL of DMF was treated with sodium methoxide (102 mg, 1.89 mmol) and the mixture stirred for 3 hours. The solution was diluted with water and extracted with 3 portions of ethyl acetate. The combined organic extracts were washed with water, brine, dried filtered and concentrated. The residue was purified by column chromatography to provide 40g (22%) of the title compound. MS (DCI, NH<sub>3</sub>): 302 (M+ NH<sub>4</sub><sup>+</sup>).

17065



17070

Example 1337B4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoic acid, methyl ester

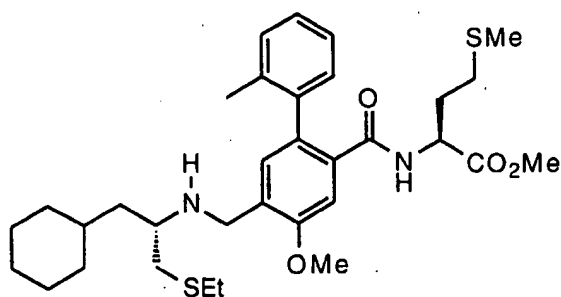
Using the procedure of example 1134E, example 1337A provided the title compound. MS (ESI +): 470 (MH<sup>+</sup>); (ESI-) 468 (M-H).

17075

Example 1337C4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoic acid

Using the procedure of example 1134F, example 1337B provided the title compound. MS (ESI +): 456 (MH<sup>+</sup>); (ESI-) 454 (M-H).

17080

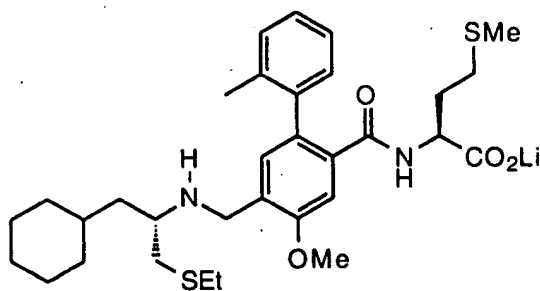
Example 1337D

17085

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine, methyl ester

According to the procedure described in example 1178I, example 1137C (55 mg, 0.12 mmol) provided 39 mg (54%) of the title compound. MS (ESI +): 601 (MH<sup>+</sup>); (ESI-) 599 (M-H).

17090

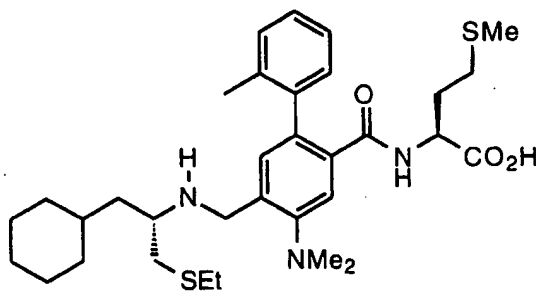
Example 1337

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine

17095

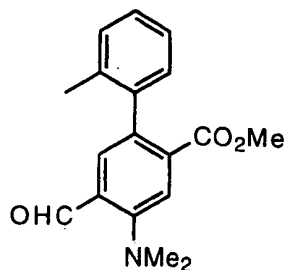
Following the procedure of example 1105D, example 1137D (39 mg, 0.065 mmol) provided the title compound. <sup>1</sup>H NMR (300 MHz, DMSO): δ 7.9 (1H), 7.0-7.3 (5H), 4.1 (1H), 3.9 (1H), 3.3 (3H), 2.7 (1H), 2.4 (3H), 2.0-2.3 (6H), 1.95 (3H), 0.8- 1.9 (22H). Mass spec (ESI): 587 (M+H), 585 (M-H)

17100

Example 1338

N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N,N'-dimethylamino-2-(2-methylphenyl)benzoyl]methionine

17105

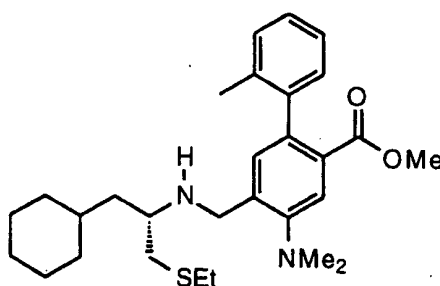


Example 1338A

2-(2-Methylphenyl)-4-formyl-5-N,N-dimethylaminobenzoic acid, methyl ester

17110 A solution of example 1134D (146 mg, 0.50 mmol) in 1 mL of DMF was treated with 2 mL of 40% aqueous dimethylamine and the mixture heated at 70°C for 2 days. The cooled reaction mixture was diluted with water and the pH of the mixture adjusted to 5. The solution was extracted with 3 portions of ethyl acetate and the combined organic extracts were washed with water and brine, dried, filtered and concentrated. The residue was dissolved in ethyl acetate and treated with ethereal diazomethane until TLC analysis indicated no more acid present. This solution was concentrated and the residue purified by column chromatography on silica gel (25 g, 15% ethyl acetate/hexanes) to provide 124 mg (87%) of the title compound. MS (DCI, NH<sub>3</sub>): 298 (MH<sup>+</sup>).

17115



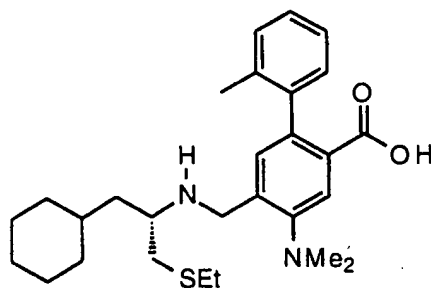
17120

Example 1338B

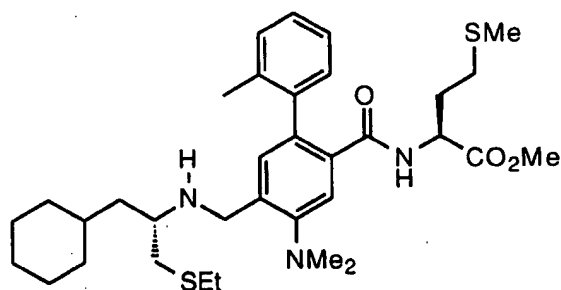
4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N,N'-dimethylamino-2-(2-methylphenyl)benzoic acid, methyl ester

Using the procedure of example 1134E, example 1338A provided the title compound. MS (ESI<sup>+</sup>): 483 (MH<sup>+</sup>); (ESI<sup>-</sup>) 481 (M-H).

17125

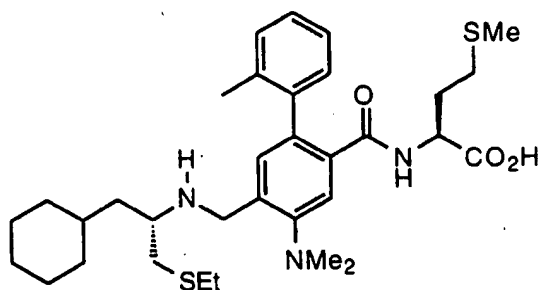
Example 1338C4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N,N'-dimethylamino-2-(2-methylphenyl)benzoic acid

17130 Following the procedure of example 1134F, example 1138B provided the title compound. MS (ESI +): 469 (MH<sup>+</sup>); (ESI-) 467 (M-H).

Example 1338D

17135 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N,N'-dimethylamino-2-(2-methylphenyl)benzoyl]methionine, methyl ester

According to the procedure described in example 1178I, example 1138C (93 mg, 0.20 mmol) provided 69 mg (56%) of the title compound. MS (ESI +): 614 (MH<sup>+</sup>); (ESI-) 612 (M-H).

Example 1338E

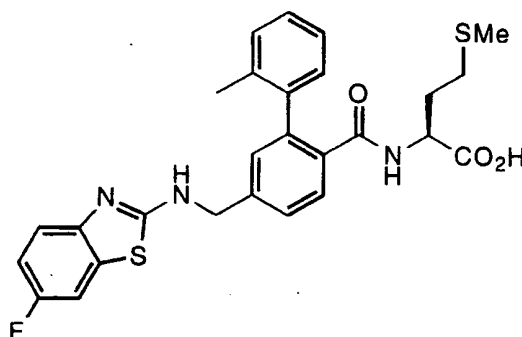
17140 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N,N'-dimethylamino-2-(2-methylphenyl)benzoyl]methionine

17145 Following the procedure of example 1105D, example 1138D (69 mg, 0.11 mmol) provided the title compound. <sup>1</sup>H NMR (300 MHz., DMSO): δ 7.9 (1H), 7.0-7.3 (5H), 4.2 (1H), 3.9 (1H), 2.72 (6H), 2.45 (3H), 2.0-2.2 (6H), 1.9 (3H), 0.7-1.85 (22H). Mass spec (ESI): 600 (M+H), 598 (M-H).

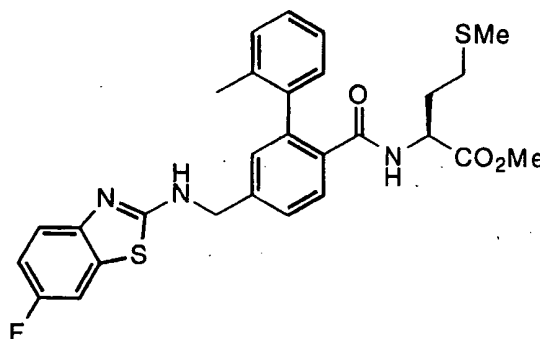
17150

Example 1339

Pittsburg example, waiting for experimental data and other information.



17155

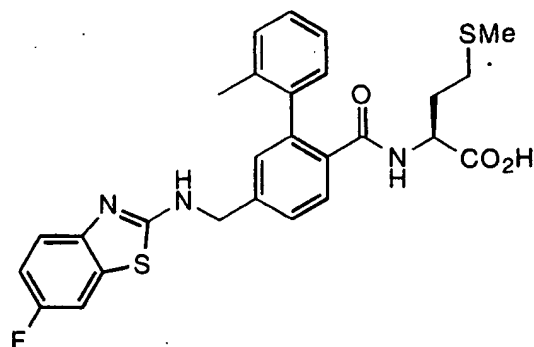
Example 1340Example 1340A

17160 N-[4-N-(6-Fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired compound was prepared according to the method of Example 1203A starting with N-[4-formyl-2-(2-methylphenyl)benzoyl]methionine methyl ester, prepared as in Example 403G, and 2-amino-6-fluorobenzothiazole. m/e (ESI) 538 (MH<sup>+</sup>)

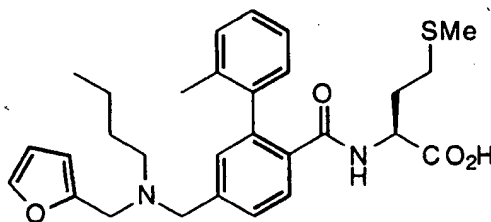
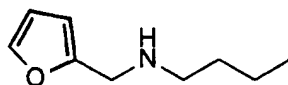
17165



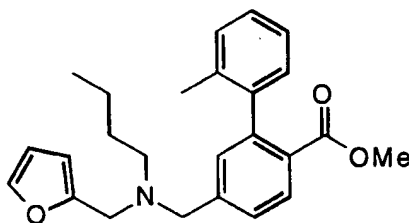
**Example 1340B***N*-[4-*N*-(6-Fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine

17170 The desired compound was prepared according to the method of Example 403I starting with the compound in Example 1340A. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.91 (1H, m), 7.51 (1H, m), 7.34 (2H, m), 7.30-7.15 (4H, m), 7.05 (3H, m), 5.99 (1H, m), 4.59 (1H, m), 4.48 (2H, bd, J=8Hz), 2.20-1.80 (9H, m), 1.72 (1H, m). m/e (ESI) 522 (MH<sup>+</sup>) Anal.calc. for C<sub>27</sub>H<sub>26</sub>FN<sub>3</sub>O<sub>3</sub>S<sub>2</sub>·0.25 H<sub>2</sub>O C 61.40, H 5.06, N 7.96 Found C 61.38, H 4.56, N 7.73

17175

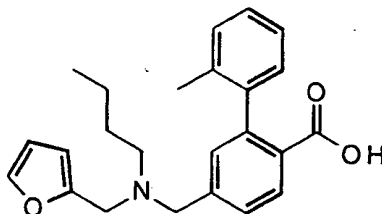
**Example 1341****Example 1341A***N*--Butyl-*N*-(furan-2-ylmethyl)amine

17180 The desired amine was prepared using the method described in Example 1171A starting with 2-furoic acid and butylamine. m/e (DCI/NH<sub>3</sub>) 154 (MH<sup>+</sup>)

**Example 1341B**

4-(*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid methyl ester

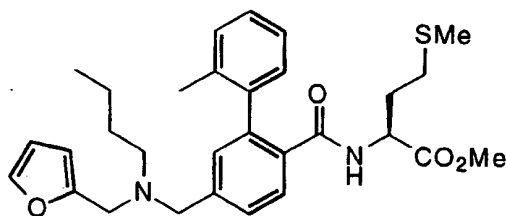
The desired compound was prepared using the method described in Example 1178G starting with *N*--Butyl-*N*-(furan-2-ylmethyl)amine, prepared as in Example 1341A, and 4-bromomethyl-2-(2-methylphenyl)benzoic acid methyl ester, prepared as in Example 1178A-D. m/e (ESI) 392 (MH<sup>+</sup>)



Example 1341C

4-(*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl)-2-(2-methylphenyl)benzoic acid

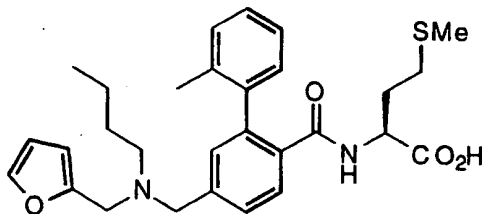
The desired acid was prepared using the method described in Example 403E starting with the compound prepared in Example 1341B.



Example 1341D

*N*-[4-*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine methyl ester

The desired product was prepared using the method described in Example 403F starting with the compound prepared in Example 1341C. m/e (ESI) 523 (MH<sup>+</sup>)



Example 1341E

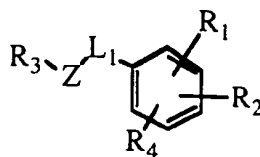
*N*-[4-*N*-Butyl-*N*-(furan-2-ylmethyl)aminomethyl]-2-(2-methylphenyl)benzoyl]methionine

The desired compound was prepared according to the method of Example 403I starting with compound prepared in Example 1341D. <sup>1</sup>H (300MHz, CDCl<sub>3</sub>, δ) 7.81 (1H,

d, J=8Hz), 7.57 (1H, m), 7.42 (1H, d, J=2Hz), 7.30-7.10 (5H, m), 6.35 (2H, m), 6.15 (1H, bd, J=8Hz), 4.43 (1H, m), 3.98 (2H, m), 3.90-3.75 (2H, m), 2.62 (2H, m), 2.20-2.00 (5H, m), 1.99 (3H, s), 1.95 (1H, m), 1.60 (3H, m), 1.29 (2H, m), 0.88 (3H, t, J=8Hz). m/e (ESI) 509 (MH<sup>+</sup>) Anal.calc. for C<sub>29</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub>S·0.50 H<sub>2</sub>O C 67.28, H 7.20, N 5.41 Found C 67.42, H 6.96, N 5.44.

WHAT IS CLAIMED IS:

- 17220 1. A compound having Formula I

**I**

or a pharmaceutically acceptable salt thereof, wherein

- 17225 **R<sub>1</sub>** is selected from the group consisting of

- (1) hydrogen,
- (2) alkenyl,
- (3) alkynyl,
- (4) alkoxy,

17230

- (5) haloalkyl,
- (6) halogen,
- (7) loweralkyl,
- (8) thioalkoxy,
- (9) aryl-L<sub>2</sub>- wherein aryl is selected from the group consisting of

17235

- (a) phenyl,
- (b) naphthyl,
- (c) dihydronaphthyl,
- (d) tetrahydronaphthyl,
- (e) indanyl, and
- (f) indenyl

17240

wherein (a)-(f) are unsubstituted or substituted with at least one of X, Y, or Z wherein X, Y, and Z are independently selected from the group consisting of

17245

alkenyl,  
alkynyl,  
alkoxy,  
aryl,  
carboxy,  
cyano,  
halogen,  
haloalkyl,

17250

hydroxy,  
hydroxyalkyl,  
loweralkyl,  
17255 nitro,  
N-protected amino, and  
-NRR' wherein R and R' are independently selected  
from the group consisting of  
hydrogen and  
17260 loweralkyl,

oxo (=O), and  
thioalkoxy and

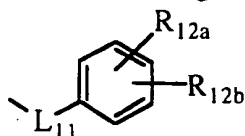
L<sub>2</sub> is absent or is selected from the group consisting of

-CH<sub>2</sub>-,  
17265 -CH<sub>2</sub>CH<sub>2</sub>-,  
-CH(CH<sub>3</sub>)-,  
-O-,  
-C(O)-,  
-S(O)<sub>q</sub> wherein q is 0, 1 or 2, and  
17270 -N(R)-, and

(10) heterocycle-L<sub>2</sub>- wherein L<sub>2</sub> is as defined above and the heterocycle is  
unsubstituted or substituted with 1, 2, 3 or 4 substituents  
independently selected from the group consisting of

- (a) loweralkyl,
- (b) hydroxy,
- (c) hydroxyalkyl,
- (d) halogen
- (e) cyano,
- (f) nitro,
- (g) oxo (=O),
- (h) -NRR',
- (i) N-protected amino,
- (j) alkoxy,
- (k) thioalkoxy,
- (l) haloalkyl,
- (m) carboxy, and
- (n) aryl;

$R_2$  is selected from the group consisting of



17290

(1) wherein  $L_{11}$  is selected from the group consisting of

- (a) a covalent bond,
- (b)  $-C(W)N(R)-$  wherein  $R$  is defined previously and  $W$  is selected from the group consisting of  $O$  and  $S$ ,
- (c)  $-C(O)-$ ,
- (d)  $-N(R)C(W)-$ ,
- (e)  $-CH_2O-$ ,
- (f)  $-C(O)O-$ , and
- (g)  $-CH_2N(R)-$ ,

17295

17300

$R_{12a}$  is selected from the group consisting of

- (a) hydrogen,
- (b) loweralkyl, and
- (c)  $-C(O)OR_{13}$  wherein  $R_{13}$  is selected from the group

17305

consisting of

hydrogen and

a carboxy-protecting group, and

$R_{12b}$  is selected from the group consisting of

- (a) hydrogen and
- (b) loweralkyl,

17310

with the proviso that  $R_{12a}$  and  $R_{12b}$  are not both hydrogen,

(2)  $-L_{11}-C(R_{14})(R_v)-C(O)OR_{15}$  wherein  $L_{11}$  is defined previously,

$R_v$  is selected from the group consisting of

- (a) hydrogen and
- (b) loweralkyl,

17315

$R_{15}$  is selected from the group consisting of

- (a) hydrogen,
- (b) alkanoyloxyalkyl,
- (c) loweralkyl, and

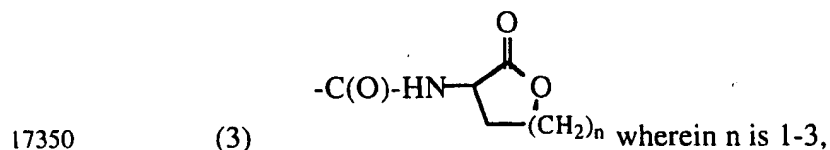
17320

(b) a carboxy-protecting group, and

$R_{14}$  is selected from the group consisting of

- (a) alkoxyalkyl,

- 17325 (b) alkoxyarylalkyl,  
(c) alkoxycarbonylalkyl,  
(d) alkylsulfinylalkyl,  
(e) alkylsulfonylalkyl,  
(f) alkynyl,  
(g) aminoalkyl,  
(h) aminocarbonylalkyl,  
17330 (i) aminothiocabonylalkyl,  
(j) aryl,  
(k) arylalkyl,  
(l) carboxyalkyl,  
(m) cyanoalkyl,  
17335 (n) cycloalkyl,  
(o) cycloalkylalkoxyalkyl,  
(p) cycloalkylalkyl,  
(q) (heterocyclic)alkyl,  
(r) hydroxyalkyl,  
17340 (s) hydroxyarylalkyl,  
(t) loweralkyl;  
(u) sulfhydrylalkyl,  
(v) thioalkoxyalkyl wherein the thioalkoxyalkyl is  
unsubstituted or substituted with 1, 2, 3, or 4  
17345 substituents selected from the group consisting of  
halogen,  
(w) thioalkoxyalkylamino, and  
(x) thiocycloalkyloxyalkyl,



- (4)  $-C(O)NH-CH(R_{14})-C(O)NHSO_2R_{16}$  wherein  $R_{14}$  is defined previously  
and  $R_{16}$  is selected from the group consisting of  
17355 (a) loweralkyl,  
(b) haloalkyl,  
(c) aryl wherein the aryl is unsubstituted or substituted with

- 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of loweralkyl, hydroxy, hydroxyalkyl, halogen, cyano, nitro, oxo (=O), -NRR', N-protected amino, alkoxy, thioalkoxy, haloalkyl, carboxy, and aryl, and
- (d) heterocycle wherein the heterocycle is unsubstituted or substituted with substituents independently selected from the group consisting of loweralkyl, hydroxy, hydroxyalkyl, halogen, cyano, nitro, oxo (=O), -NRR', N-protected amino, alkoxy, thioalkoxy, haloalkyl, carboxy, and aryl;
- (5) -C(O)NH-CH(R<sub>14</sub>)-tetrazolyl wherein the tetrazole ring is unsubstituted or substituted with loweralkyl or haloalkyl,



(6) -L<sub>11</sub>-heterocycle,

17395

(7) -C(O)NH-CH(R<sub>14</sub>)-C(O)NR<sub>17</sub>R<sub>18</sub> wherein R<sub>14</sub> is defined previously and R<sub>17</sub> and R<sub>18</sub> are independently selected from the group consisting of

17400

- (a) hydrogen,
- (b) loweralkyl,
- (c) arylalkyl,
- (d) hydroxy, and
- (e) dialkylaminoalkyl,

17405

(8) -C(O)OR<sub>15</sub>, and

(9) -C(O)NH-CH(R<sub>14</sub>)-heterocycle wherein R<sub>14</sub> is as previously defined and the heterocycle is unsubstituted or substituted with loweralkyl or haloalkyl;

17410

L<sub>1</sub> is absent or is selected from the group consisting of

(1) -L<sub>4</sub>-N(R<sub>5</sub>)-L<sub>5</sub>- wherein L<sub>4</sub> is absent or selected from the group consisting of

17415

- (a) C<sub>1</sub>-to-C<sub>10</sub>-alkylene and
- (b) C<sub>2</sub>-to-C<sub>16</sub>-alkenylene,

wherein the alkylene and alkenylene groups are unsubstituted or substituted with 1, 2, 3 or 4 substituents independently selected from the group consisting of

17420

alkenyl,  
alkenyloxy,  
alkenyloxyalkyl,  
alkenyl[S(O)<sub>q</sub>]alkyl,  
alkoxy,

alkoxyalkyl wherein the alkoxyalkyl is unsubstituted or substituted with 1 or 2 hydroxyl substituents, with the proviso that no two hydroxyls are attached to the same carbon,

17425

alkoxycarbonyl wherein the alkoxycarbonyl is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from the

17430

- group consisting of  
halogen and  
cycloalkyl,  
alkylsilyloxy,  
17435 alkyl[S(O)<sub>q</sub>],  
alkyl[S(O)<sub>q</sub>]alkyl,  
aryl wherein the aryl is unsubstituted or substituted with  
1, 2, 3, 4, or 5 substituents independently  
selected from the group consisting of  
17440 alkoxy wherein the alkoxy is unsubstituted or  
substituted with substituents selected  
from the group consisting of cycloalkyl,  
aryl,  
arylalkyl,  
17445 aryloxy wherein the aryloxy is unsubstituted or  
substituted with 1, 2, 3, 4, or 5  
substituents independently selected from  
the group consisting of,  
halogen,  
17450 nitro, and  
-NRR',  
cycloalkyl,  
halogen,  
loweralkyl,  
17455 hydroxyl,  
nitro,  
-NRR', and  
-SO<sub>2</sub>NRR',  
arylalkoxy wherein the arylalkoxy is unsubstituted or  
17460 substituted with substituents selected from the  
group consisting of alkoxy,  
arylalkyl,  
arylalkyl[S(O)<sub>q</sub>]alkyl,  
aryl[S(O)<sub>q</sub>],  
17465 aryl[S(O)<sub>q</sub>]alkyl wherein the aryl[S(O)<sub>q</sub>]alkyl is  
unsubstituted or substituted with 1, 2, 3, 4, or 5  
substituents independently selected from

- alkoxy and  
loweralkyl,  
17470 arylalkoxyalkyl wherein the arylalkoxyalkyl is  
unsubstituted or substituted with substituents  
selected from the group consisting of  
alkoxy, and  
halogen,
- 17475 aryloxy,  
aryloxyalkyl wherein the aryloxyalkyl is unsubstituted or  
substituted with substituents selected from the  
group consisting of halogen,
- 17480 carboxyl,  
-C(O)NR<sub>C</sub>R<sub>D</sub> wherein R<sub>C</sub> and R<sub>D</sub> are independently  
selected from the group consisting of  
hydrogen,  
loweralkyl, and  
alkoxycarbonyl or
- 17485 R<sub>C</sub> and R<sub>D</sub> together with the nitrogen to which  
they are attached form a ring selected  
from the group consisting of  
morpholine,  
piperidine,  
17490 pyrrolidine  
thiomorpholine,  
thiomorpholine sulfone, and  
thiomorpholine sulfoxide,  
wherein the ring formed by R<sub>C</sub> and R<sub>D</sub>
- 17495 together is unsubstituted or  
substituted with 1 or 2  
substituents independently  
selected from the group consisting  
of alkoxy and alkoxyalkyl,
- 17500 cycloalkenyl wherein the cycloalkenyl is unsubstituted or  
substituted with 1 or 2 substituents selected from  
the group consisting of alkenyl,  
cyclolalkoxy,  
cycloalkoxycarbonyl,

- 17505 cyclolalkoxyalkyl,  
cycloalkyl wherein the cycloalkyl is unsubstituted or  
substituted with 1, 2, 3, 4, or 5 substituents  
independently selected from the group consisting  
of aryl,
- 17510 loweralkyl, and  
alkanoyl,  
cycloalkylalkoxy,  
cycloalkylalkoxycarbonyl,  
cycloalkylalkoxyalkyl,
- 17515 cycloalkylalkyl,  
cycloalkyl[S(O)<sub>q</sub>]alkyl,  
cycloalkylalkyl[S(O)<sub>q</sub>]alkyl,  
fluorenyl,  
heterocycle wherein the heterocycle is unsubstituted or  
substituted with 1, 2, 3, or 4 substituents  
independently selected from the group  
consisting of  
alkoxy wherein the alkoxy is unsubstituted or  
substituted with 1 or 2 substituents  
independently selected from the group  
consisting of aryl and cycloalkyl,
- 17525 alkoxyalkyl wherein the alkoxyalkyl is  
unsubstituted or substituted with 1 or 2  
substituents independently selected from  
the group consisting of  
aryl and  
cycloalkyl,
- 17530 alkoxycarbonyl wherein the alkoxycarbonyl is  
unsubstituted or substituted with 1 or 2  
substituents independently selected from  
the group consisting of  
aryl and  
cycloalkyl,
- 17535 aryl wherein the aryl is unsubstituted or  
substituted with 1, 2, 3, 4, or 5  
substituents independently selected from
- 17540

- 17545 the group consisting of  
alkanoyl,  
alkoxy,  
carboxaldehyde,  
haloalkyl,  
halogen,  
loweralkyl,  
nitro,  
17550 -NRR', and  
thioalkoxy,  
arylalkyl,  
aryloxy,  
cycloalkoxyalkyl,  
17555 cycloalkyl,  
cycloalkylalkyl,  
halogen,  
heterocycle,  
hydroxyl,  
17560 loweralkyl wherein the loweralkyl is  
unsubstituted or substituted with 1, 2, or  
3 substituents independently selected  
from the group consisting of  
heterocycle,  
17565 hydroxyl,  
with the proviso that no two hydroxyls  
are attached to the same carbon,  
and  
-NR<sup>R3</sup>R<sup>R3'</sup> wherein R<sup>R3</sup> and R<sup>R3'</sup> are  
17570 independently selected from the  
group consisting of  
hydrogen  
aryl,  
loweralkyl,  
17575 aryl,  
arylalkyl,  
heterocycle,  
(heterocyclic)alkyl,

- 17580 cycloalkyl, and  
cycloalkylalkyl, and  
sulfhydryl,  
(heterocyclic)alkoxy,  
(heterocyclic)alkyl,  
(heterocyclic)alkyl[S(O)<sub>q</sub>]alkyl,
- 17585 (heterocyclic)oxy,  
(heterocyclic)alkoxyalkyl,  
(heterocyclic)oxyalkyl,  
heterocycle[S(O)<sub>q</sub>]alkyl,  
hydroxyl,
- 17590 hydroxyalkyl,  
imino,  
N-protected amino,  
=N-O-aryl, and  
=N-OH,
- 17595 =N-O-heterocycle wherein the heterocycle is  
unsubstituted or substituted with 1, 2, 3, or 4  
substituents independently selected from the  
group consisting of  
loweralkyl,
- 17600 hydroxy,,  
hydroxyalkyl,  
halogen,  
cyano,  
nitro,
- 17605 oxo (=O),  
-NRR'  
N-protected amino,  
alkoxy,  
thioalkoxy,
- 17610 haloalkyl,  
carboxy, and  
aryl,  
=N-O-loweralkyl,  
-NRR<sup>3</sup>R<sup>3</sup>',
- 17615 -NHNR<sub>C</sub>R<sub>D</sub>,

-OG wherein G is a hydroxyl protecting group,

-O-NH-R<sub>1</sub>,

$\text{-O-N}=\begin{matrix} \text{J}' \\ \text{J} \end{matrix}$  wherein J and J' are independently selected

from the group consisting of

17620

loweralkyl and

arylalkyl,

oxo,

oxyamino(alkyl)carbonylalkyl,

oxyamino(arylalkyl)carbonylalkyl,

17625

oxyaminocarbonylalkyl,

-SO<sub>2</sub>-A wherein A is selected from the group

consisting of

loweralkyl,

aryl, and

17630

heterocycle

wherein the loweralkyl, aryl, and heterocycle are

unsubstituted or substituted with 1, 2, 3,

4, or 5 substituents independently

selected from the group consisting of

17635

alkoxy,

halogen,

haloalkyl,

loweralkyl, and

nitro,

17640

sulfhydryl,

thioxo, and

thioalkoxy,

L<sub>5</sub> is absent or selected from the group consisting of

(a) C<sub>1</sub>-to-C<sub>10</sub>-alkylene and

17645

(b) C<sub>2</sub>-to-C<sub>16</sub>-alkenylene

wherein (a) and (b) are unsubstituted or substituted as

defined previously, and

R<sub>5</sub> is selected from the group consisting of

hydrogen,

17650

alkanoyl wherein the alkanoyl is unsubstituted or

substituted with substituents selected from the

- group consisting of aryl,  
alkoxy,  
alkoxyalkyl,  
17655 alkoxycarbonyl wherein the alkoxycarbonyl is  
unsubstituted or substituted with 1, 2 or 3  
substituents independently selected from the  
group consisting of  
aryl and  
17660 halogen,  
alkylaminocarbonylalkyl wherein the  
alkylaminocarbonylalkyl is unsubstituted or  
substituted with 1 or 2 substituents  
independently selected from the group consisting  
17665 of aryl,  
(anthracenyl)alkyl,  
aryl,  
arylalkoxy,  
arylalkyl wherein the arylalkyl is unsubstituted or  
17670 substituted with 1, 2, 3, 4, or 5 substituents  
independently selected from the group  
consisting of  
alkoxy,  
aryl,  
17675 carboxyl,  
cyano,  
halogen,  
haloalkoxy,  
haloalkyl,  
17680 nitro,  
oxo, and  
-L<sub>11</sub>-C(R<sub>14</sub>)(R<sub>v</sub>)-C(O)OR<sub>15</sub>,  
(aryl)oyl wherein the (aryl)oyl is unsubstituted or  
substituted with substituents selected from the  
17685 group consisting of halogen,  
aryloxycarbonyl,  
carboxaldehyde,  
-C(O)NRR',



- 17690 cycloalkoxycarbonyl,  
cycloalkylaminocarbonyl,  
cycloalkylaminothiocarbonyl,  
cyanoalkyl,  
cyclolalkyl,  
cycloalkylalkyl wherein the cycloalkylalkyl is
- 17695 unsubstituted or substituted with 1 or 2 hydroxyl  
substituents,  
with the proviso that no two hydroxyls are attached to the  
same carbon,  
(cyclolalkyl)oyl,
- 17700 (9,10-dihydroanthracenyl)alkyl wherein the  
(9,10-dihydroanthracenyl)alkyl is unsubstituted  
or substituted with 1 or 2 oxo substituents,  
haloalkyl,  
heterocycle,
- 17705 (heterocyclic)alkyl wherein the (heterocyclic)alkyl is  
unsubstituted or substituted with 1, 2, 3, 4, or 5  
substituents selected from the group consisting of  
loweralkyl,  
(heterocyclic)oyl,
- 17710 loweralkyl, wherein the loweralkyl is unsubstituted  
or substituted with substituents selected from the  
group consisting of -NRR',  
-SO<sub>2</sub>-A, and  
thioalkoxyalkyl;
- 17715
- (2) -L<sub>4</sub>-O-L<sub>5</sub>-,
- (3) -L<sub>4</sub>-S(O)<sub>m</sub>-L<sub>5</sub>- wherein L<sub>4</sub> and L<sub>5</sub> are defined previously and m is 0, 1,  
or 2,
- 17720
- (4) -L<sub>4</sub>-L<sub>6</sub>-C(W)-N(R<sub>6</sub>)-L<sub>5</sub>- wherein L<sub>4</sub>, W, and L<sub>5</sub> are defined previously,  
R<sub>6</sub> is selected from the group consisting of
- (a) hydrogen,
- (b) loweralkyl,
- 17725 (c) aryl,

- (d) arylalkyl,  
 (e) heterocycle,  
 (f) (heterocyclic)alkyl,  
 (g) cyclolakyl, and  
 (h) cycloalkylalkyl, and  
 L<sub>6</sub> is absent or is selected from the group consisting of  
 (a) -O-,  
 (b) -S-, and  
 (c) -N(R<sub>6</sub>)- wherein R<sub>6</sub> is selected from the group  
 consisting of  
 hydrogen,  
 loweralkyl,  
 aryl,  
 arylalkyl,  
 heterocycle,  
 (heterocyclic)alkyl,  
 cyclolakyl, and  
 cycloalkylalkyl,
- 17730
- 17735
- 17740
- 17745 (5) -L<sub>4</sub>-L<sub>6</sub>-S(O)<sub>m</sub>-N(R<sub>5</sub>)-L<sub>5</sub>-,  
 (6) -L<sub>4</sub>-L<sub>6</sub>-N(R<sub>5</sub>)-S(O)<sub>m</sub>-L<sub>5</sub>-,  
 (7) -L<sub>4</sub>-N(R<sub>5</sub>)-C(W)-L<sub>7</sub>-L<sub>5</sub>- wherein L<sub>4</sub>, R<sub>5</sub>, W, and L<sub>5</sub> are  
 17750 defined previously and L<sub>7</sub> is absent or is selected from the group  
 consisting of -O- and -S-,  
 (8) C<sub>1</sub>-C<sub>10</sub>-alkylene wherein the alkylene group is unsubstituted or  
 substituted with 1 or 2 substituents independently selected from  
 17755 the group consisting of  
 (a) aryl,  
 (b) arylalkyl,  
 (c) heterocycle,  
 (d) (heterocyclic)alkyl,  
 17760 (e) cyclolakyl,  
 (f) cycloalkylalkyl,  
 (g) alkylthioalkyl, and

(h) hydroxy,

17765

(9) C<sub>2</sub>-to-C<sub>10</sub>-alkenylene wherein the alkenylene group is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of

(a) aryl,

(b) arylalkyl,

17770

(c) (aryl)oxyalkyl wherein the (aryl)oxyalkyl is

unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen,

(d) heterocycle,

17775

(e) (heterocycle)alkyl,

(f) hydroxyalkyl,

(g) cyclolalkyl,

(h) cycloalkylalkyl,

(i) alkylthioalkyl, and

17780

(j) hydroxy,

(10) C<sub>2</sub>-to-C<sub>10</sub>-alkynylene wherein the alkynylene group is unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of

17785

(a) aryl,

(b) arylalkyl,

(c) heterocycle,

(d) (heterocyclic)alkyl,

(e) cyclolalkyl,

17790

(f) cycloalkylalkyl,

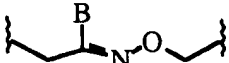
(g) alkylthioalkyl, and

(h) hydroxy,

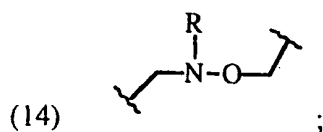
(11) -L<sub>4</sub>-heterocycle-L<sub>5</sub>-,

17795

(12) a covalent bond,

(13)  wherein B is selected from the group consisting of

loweralkyl and  
arylalkyl, and



**Z** is selected from the group consisting of

- (1) a covalent bond,
- (2) -O-,
- (3) -S(O)<sub>q</sub>-, and
- (4) -NR<sub>Z</sub>- wherein R<sub>Z</sub> is selected from the group consisting of
  - (a) hydrogen
  - (b) loweralkyl,
  - (c) aryl,
  - (d) arylalkyl,
  - (e) heterocycle,
  - (f) (heterocyclic)alkyl,
  - (g) cyclolalkyl, and
  - (h) cycloalkylalkyl;

**R<sub>3</sub>** is selected from the group consisting of

- (1) hydrogen,
- (2) aryl,
- (3) fluorenyl,
- (4) heterocycle,

with the proviso that the heterocycle is other than imidazole and pyridine,

wherein (2)-(4) are unsubstituted or substituted with 1, 2, 3, 4, or 5

substituents independently selected from the group consisting of

- (a) alkanoyl,
- (b) alkoxy wherein the alkoxy is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of
 

halogen,  
aryl, and  
cycloalkyl,
- (c) alkoxyalkyl wherein the alkoxyalkyl is unsubstituted or substituted with 1 or 2, 3, 4 or 5 substituents

- 17835 independently selected from the group consisting of  
aryl and  
cycloalkyl,
- (d) alkoxycarbonyl wherein the alkoxycarbonyl is unsubstituted or  
substituted with 1, 2, 3, 4, or 5 substituents  
independently selected from the group consisting of  
17840 aryl, and  
cycloalkyl,
- (e) alkylsilyloxyalkyl,
- (f) arylalkyl,
- (g) aryl wherein the aryl is unsubstituted or substituted with 1, 2, 3,  
17845 4, or 5 substituents independently selected from the  
group consisting of  
alkanoyl,  
alkoxy wherein the alkoxy is unsubstituted or substituted  
with 1 or 2 substituents selected from the group  
17850 consisting of cycloalkyl,  
carboxaldehyde,  
haloalkyl,  
halogen,  
loweralkyl,  
17855 nitro,  
-NRR', and  
thioalkoxy,
- (h) arylalkyl,
- (i) aryloxy wherein the aryloxy is unsubstituted or  
17860 substituted with 1, 2, 3, 4, or 5 substituents  
independently selected from the group consisting of,  
halogen,  
nitro, and  
-NRR',
- (j) (aryl)oyl,
- (k) carboxaldehyde,
- (l) carboxy,
- (m) carboxyalkyl,
- (n) -C(O)NRR" wherein R is defined previously and R" is  
17870 selected from the group consisting of

- hydrogen,  
loweralkyl, and  
carboxyalkyl,
- 17875 (o) cyano,  
(p) cyanoalkyl,  
(q) cycloalkyl,  
(r) cycloalkylalkyl,  
(s) cycloalkoxyalkyl,  
(t) halogen,
- 17880 (u) haloalkyl wherein the haloalkyl is unsubstituted or substituted  
with 1, 2, 3, 4, or 5 hydroxyl substituents,  
with the proviso that no two hydroxyls are attached to the same  
carbon,
- 17885 (v) heterocycle,  
(w) hydroxyl,  
(x) hydroxyalkyl wherein the hydroxyalkyl is unsubstituted or  
substituted with substituents selected from the group  
consisting of aryl,
- 17890 (y) loweralkyl wherein the loweralkyl is unsubstituted or substituted  
with substituents selected from the group consisting of  
heterocycle,  
hydroxyl,  
with the proviso that no two hydroxyls are attached to the  
same carbon,
- 17895 -NRR<sup>3</sup>RR<sup>3'</sup>, and  
-P(O)(OR)(OR'),
- (z) nitro,  
(aa) -NRR',  
(bb) oxo,
- 17900 (cc) -SO<sub>2</sub>NR<sub>A</sub>'R<sub>B</sub>' wherein R<sub>A</sub>' and R<sub>B</sub>' are independently selected  
from the group consisting of  
hydrogen,  
(aryl)oyl,  
loweralkyl, and
- 17905 heterocycle wherein the heterocycle is unsubstituted or  
substituted with 1, 2, or 3 substituents  
independently selected from the group consisting

of loweralkyl,

(dd) sulfhydryl, and

17910

(ee) thioalkoxy,

(5) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted with 1, 2, 3, 4 or 5 substituents selected from the group consisting of

17915

(a) alkoxy,

(b) aryl,

(c) arylalkoxy

(d) aryloxy wherein the aryloxy is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen,

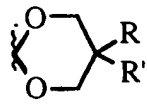
17920

(e) loweralkyl,

(f) halogen,

(g)  $\text{NR}^3\text{R}^3'$ ,

(h) oxo, and

(i) 

17925

(6) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted with 1, 2, 3 or 4 substituents independently selected from the group consisting of

(a) loweralkyl,

17930

(b) alkoxy,

(c) halogen,

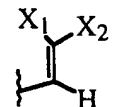
(d) aryl,

(e) aryloxy,

(f) alkanoyl, and

17935

(g)  $\text{NR}^3\text{R}^3'$ ,

(7)  wherein  $\text{X}_1$  and  $\text{X}_2$  together are cycloalkyl wherein the cycloalkyl is unsubstituted or substituted with 1 or 2 substituents selected from the group consisting of aryl, and

17940

(8)  $-\text{P}(\text{W})\text{R}^3\text{R}^3'$ ; and

**R<sub>4</sub>** is selected from the group consisting of

- (1) hydrogen,
- (2) loweralkyl,
- (3) haloalkyl
- (4) halogen,
- (5) aryl,
- (6) arylalkyl,
- (7) heterocycle,
- (8) (heterocyclic)alkyl
- (9) alkoxy, and
- (10) -NRR'; or

**L<sub>1</sub>, Z, and R<sub>3</sub>** together are selected from the group consisting of

- (1) aminoalkyl,
- (1) haloalkyl,
- (2) halogen,
- (3) carboxaldehyde, and
- (4) (carboxaldehyde)alkyl, and
- (5) hydroxyalkyl,

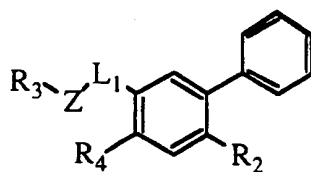
with the proviso that when **L<sub>1</sub>, Z, and R<sub>3</sub>** together are (1)-(5), **R<sub>1</sub>** is other than hydrogen.

2. A compound according to claim 1 wherein **L<sub>1</sub>** is selected from the group consisting of

- (1) -L<sub>4</sub>-N(R<sub>5</sub>)-L<sub>5</sub>-,
- (2) -L<sub>4</sub>-L<sub>6</sub>-C(W)-N(R<sub>6</sub>)-L<sub>5</sub>-, and
- (3) -L<sub>4</sub>-N(R<sub>5</sub>)-C(W)-L<sub>7</sub>-L<sub>5</sub>- and

**Z** is a covalent bond or -O-.

3. A compound according to claim 1 of formula



wherein



**R<sub>3</sub>** is selected from the group consisting of

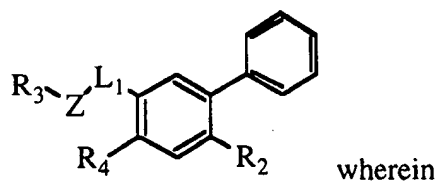
- 5 (1) hydrogen,
- (2) aryl,
- (3) heterocycle,
- (3) fluorenyl,
- wherein (2)-(4) are unsubstituted or substituted as defined previously,
- 10 (4) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and
- (5) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

15 **L<sub>1</sub>** is selected from the group consisting of

- (1) -L<sub>4</sub>-N(R<sub>5</sub>)-L<sub>5</sub><sup>-</sup>,
- (2) -L<sub>4</sub>-L<sub>6</sub>-C(W)-N(R<sub>6</sub>)-L<sub>5</sub><sup>-</sup>, and
- (3) -L<sub>4</sub>-N(R<sub>5</sub>)-C(W)-L<sub>7</sub>-L<sub>5</sub><sup>-</sup>; and

20 **Z** is a covalent bond or -O-.

4. A compound according to claim 1 of formula



**R<sub>3</sub>** is selected from the group consisting of

- 5 (1) hydrogen,
- (2) aryl,
- (3) fluorenyl,
- wherein (2) and (3) are unsubstituted or substituted as defined previously,
- (4) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and
- 10 (5) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

**L<sub>1</sub>** is selected from the group consisting of

- 15 (1) -L<sub>4</sub>-N(R<sub>5</sub>)-L<sub>5</sub><sup>-</sup>,
- (2) -L<sub>4</sub>-L<sub>6</sub>-C(W)-N(R<sub>6</sub>)-L<sub>5</sub><sup>-</sup>, and

(3)  $-L_4-N(R_5)-C(W)-L_7-L_5-$ ; and

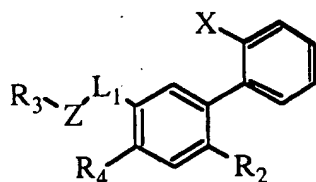
Z is a covalent bond or -O-.

20

5. A compound according to claim 4 selected from the group consisting of
- [4-(thiazo-4-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - [4-(thiazol-2-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - [4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - 5 methyl ester, hydrochloride,
  - [4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - [4-((R)-thiazolidin-4-ylmethyl)amino-2-phenylbenzoyl]methionine,
  - hydrochloride,
  - [4-(4-hydroxy-prolinyl)amino-2-phenylbenzoyl]methionine, trifluoroacetate,
  - 10 [4-((2S,4S)-4-mercaptopyrrolidin-2-carboxy)amino-2-phenylbenzoyl]-
  - methionine, trifluoroacetate,
  - [4-((2S,4R)-4-hydroxypyrrolidin-2-ylmethyl)amino-2-phenylbenzoyl]-
  - methionine, hydrochloride,
  - [4-((2S,4S)-4-thiopyrrolidin-2-yl-methylamino)-2-phenylbenzoyl]-methionine,
  - 15 hydrochloride,
  - [4-(1H-benzimidazol-5-ylcarboxyamino)-2-phenylbenzoyl]methionine,
  - trifluoroacetate,
  - [4-(piperidin-2-ylcarboxyamino)-2-phenylbenzoyl]methionine,
  - hydrochloride,
  - 20 [4-(2-pyrrolidinone-5-ylcarbonylamino)-2-phenylbenzoyl]methionine,
  - [4-(5-pyrimidylcarboxyamino)-2-phenylbenzoyl]methionine,
  - [4-(3-piperidinecarboxyamino)-2-phenylbenzoyl]methionine,
  - hydrochloride,
  - [4-(1H-4-trifluoromethyl-1,2-dihydropyrid-3-ylcarbonylamino)-2-
  - 25 phenylbenzoyl]methionine, sodium salt,
  - [4-(2-piperazinylmethylamino)-2-phenylbenzoyl]methionine,
  - [4-(2-furylmethylaminomethyl)-2-phenylbenzoyl]methionine lithium salt,
  - N-[4-N-2-hydroxyethylamino-2-phenylbenzoyl]methionine,
  - N-[4-(N-2-amino-3-benzoyloxypropionyl)amino-2-phenylbenzoyl]methionine,
  - 30 N-[4-N-phenyl-N-benzylaminomethyl-2-phenylbenzoyl]methionine,
  - N-[4-N-(2-hydroxyethyl)-N-benzylaminomethyl-2-
  - phenylbenzoyl]methionine, lithium salt,

N-[4-N-(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,  
 N-[4-N,N-dibenzylaminomethyl-2-phenylbenzoyl]methionine, lithium salt,  
 35 N-[4-N-(benzyl-N-thiazol-5-ylmethyl)aminomethyl-2-phenylbenzoyl]-  
 methionine,  
 N-[4-(N-benzylaminomethyl)-2-phenylbenzoyl]methionine, hydrochloride salt,  
 N-[4-(4-hydroxyprolinylamino)-2-phenylbenzoyl]methionine,  
 N-[4-((2S,4S)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine,  
 40 N-[4-((2S,4R)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine, and  
 N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-phenylbenzoyl]-  
 methionine, lithium salt.

6. A compound according to claim 1 of formula



wherein

**R<sub>3</sub>** is selected from the group consisting of

- (1) hydrogen,
- (2) aryl,
- (3) fluorenyl,
- (4) heterocycle

wherein (2)-(4) are unsubstituted or substituted as defined previously,

- (5) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as defined previously, and
- (6) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as defined previously;

**L<sub>1</sub>** is selected from the group consisting of

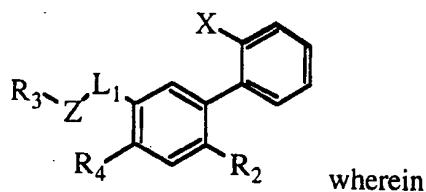
- (1)  $-\text{L}_4-\text{N}(\text{R}_5)-\text{L}_5-$ ,
- (2)  $-\text{L}_4-\text{L}_6-\text{C}(\text{W})-\text{N}(\text{R}_6)-\text{L}_5-$ , and
- (3)  $-\text{L}_4-\text{N}(\text{R}_5)-\text{C}(\text{W})-\text{L}_7-\text{L}_5-$ ;

**Z** is a covalent bond or -O-; and

**X** is selected from the group consisting of  
alkoxy,

25 aryl,  
 25 carboxy,  
 cyano,  
 halogen,  
 haloalkyl,  
 hydroxy,  
 30 hydroxyalkyl,  
 loweralkyl,  
 nitro,  
 N-protected amino,  
 -NRR,  
 35 oxo (=O), and  
 thioalkoxy.

7. A compound according to claim 1 of formula



**R<sub>3</sub>** is selected from the group consisting of

- 5 (1) hydrogen,  
 (2) aryl,  
 (3) fluorenyl,

wherein (2) and (3) are unsubstituted or substituted as defined previously,

- (4) cycloalkyl wherein the cycloalkyl is unsubstituted or substituted as  
 10 defined previously, and  
 (5) cycloalkenyl wherein the cycloalkenyl is unsubstituted or substituted as  
 defined previously;

**L<sub>1</sub>** is selected from the group consisting of

- 15 (1) -L<sub>4</sub>-N(R<sub>5</sub>)-L<sub>5</sub>-,  
 (2) -L<sub>4</sub>-L<sub>6</sub>-C(W)-N(R<sub>6</sub>)-L<sub>5</sub>-, and  
 (3) -L<sub>4</sub>-N(R<sub>5</sub>)-C(W)-L<sub>7</sub>-L<sub>5</sub>-;

**Z** is a covalent bond or -O-; and

20

X is selected from the group consisting of

alkoxy,  
 aryl,  
 carboxy,  
 cyano,  
 halogen,  
 haloalkyl,  
 hydroxy,  
 hydroxyalkyl,  
 loweralkyl,  
 nitro,  
 N-protected amino,  
 -NRR,  
 oxo (=O), and  
 thioalkoxy.

8. A compound according to claim 6 wherein X is selected from the group consisting of loweralkyl, halogen, and haloalkyl.
9. A compound according to claim 8 selected from the group consisting of  
 [4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-  
 benzoyl]methionine,  
 4-(N-benzyl-N-phenyl)-aminomethyl-2-(2-methylphenyl)benzoylmethionine,  
 N-[4-N-(2,2-dibenzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-  
 methionine, sodium salt,  
 N-[4-N-(2-benzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-  
 methionine, sodium salt,  
 N-[4-N-(2-cyclohexylmethyl-3-hydroxypropyl)amino-2-(2-methylphenyl)-  
 benzoyl]methionine,  
 N-[4-N-(furan-2-ylmethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-  
 methionine, lithium salt,  
 N-[4-N-(2-benzylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
 N-[4-N-(2-phenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
 methionine,  
 N-[4-N-(3-phenyl)propyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
 methionine,  
 N-[4-N-(2,2-diphenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)-

- benzoyl]methionine,
- 20 N-[4-N-(adamantan-1-ylmethyl)-N-phenyl]aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,
- N-[4-N-(2-adamantan-1-ylethyl)-N-phenyl]aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,
- N-[4-N,N-dibenzylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- 25 lithium salt,
- N-[4-N-(2-phenylethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,
- N-[4-N-(3-phenoxybenzyl)-N-benzylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- 30 N-[4-N-methyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,
- N-[4-N-benzyl-N-pyrazin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,
- N-[4-N-(2-phenylethyl)-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- 35 N-[4-N-(2-indol-3-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,
- N-[4-N-(2-cyclohexyl-1-ethan-1-ol-2-yl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- 40 N-[4-N-(1,3-diphenylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,
- N-[4-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- N-[4-N-(1-cyclohexyl-6-methylhept-3-en-2-yl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,
- 45 N-[4-N-(1-cyclohexyl-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-  
2-(2-methylphenyl)benzoyl]methionine,
- 50 N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-  
2-(2-methylphenyl)benzoyl]methionine,
- N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, methyl ester,
- 55

N-[4-N-phenylacetyl-amino-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,

N-[4-N-(4'-methylphenylacetyl)amino-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,

60 N-[4-N-(4'-methoxyphenylacetyl)amino-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,

N-[4-N-(3-phenylpropionoyl)amino-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,

65 N-[4-N-(3-(2-methoxyphenyl)propionoyl)amino-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,

N-[4-N-benzyl-N-(thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,

N-[4-N-benzyl-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,

70 N-[4-(2-cyclohexylethan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,

N-[4-(N-benzyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,

75 N-[4-(N-2-cyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, trifluoroacetate salt,

N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,

N-[4-(N-acetyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,

80 N-[4-(N-(N,N-dimethylaminocarbonyl)-N-(2-cyclohexylethyl)-  
aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,

N-[4-(N-(2-cyclohexylethyl)-N-methanesulfonylaminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,

85 N-[4-(N-benzenesulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine lithium salt,

N-[4-(3-cyclohexylpropan-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine,

N-[4-(4-cyclohexylbutan-3-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,

90 N-[4-(6-cyclohexylhexan-5-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,

N-[4-(1,2-dicyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-

- methionine, lithium salt,  
 95 N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
 methionine,  
 N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
 methionine, trifluoroacetate salt,  
 N-[4-(2-cyclohexylprop-1-en-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
 methionine, lithium salt,  
 100 N-[4-(3-cyclohexyl-1-ethylsulfonyl)propan-2-ylaminomethyl)-2-(2-methyl-  
 phenyl)benzoyl]methionine, lithium salt,  
 N-[4-(3-cyclohexyl-1-ethylsulfonyl)propan-2-ylaminomethyl)-2-(2-methyl-  
 phenyl)benzoyl]-2-amino-4-methanesulfonylbutanoic acid, lithium salt,  
 N-[4-(3-cyclohexyl-1-t-butylthioprop-2-ylaminomethyl)-2-(2-methylphenyl)-  
 105 benzoyl]methionine, lithium salt,  
 N-[4-(3-cyclohexyl-1-phenylthioprop-2-ylaminomethyl)-2-(2-methylphenyl)-  
 benzoyl]methionine, lithium salt,  
 N-[4-N-benzoyl-N-2-cyclohexylethylaminomethyl-2-(2-methylphenyl)benzoyl]-  
 methionine, lithium salt,  
 110 N-[4-N-t-butyloxycarbonyl-N-2-cyclohexylethylaminomethyl-2-(2-methyl-  
 phenyl)benzoyl]methionine, lithium salt,  
 pivaloyloxymethyl N-[4-N-(3-cyclohexyl-1-ethylthioprop-2-yl)-N-methyl-  
 aminomethyl-2-(2-methylphenyl)benzoyl]methionine, hydrochloride salt,  
 N-[4-N-(3-cyclohexyl-1-ethylthioprop-2-yl)-N-methylaminomethyl-2-  
 115 (2-methylphenyl)benzoyl]-N-methylmethionine, lithium salt,  
 N-[4-N-(3-cyclohexyl-1-cyclohexylthioprop-2-yl)-N-methylamino-  
 methyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(3-cyclohexyl-1-(2-methylphenyl)thioprop-2-yl)-N-methyl-  
 aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 120 N-[4-N-(N-phenyl-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)-  
 benzoyl]methionine, lithium salt,  
 N-[4-N-(N-phenyl-N-toluenesulfonylaminomethyl)-2-(2-methylphenyl)-  
 benzoyl]methionine, lithium salt,  
 N-[4-N-(N-phenyl-N-(3-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-  
 125 benzoyl]methionine, lithium salt,  
 N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzenesulfonyl)aminomethyl)-  
 2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-phenyl-N-(4-chlorobenzyl)aminomethyl)-2-(2-methylphenyl)-  
 benzoyl]methionine, lithium salt,



- 130 N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,  
N-[4-(1-ethoxycarbonylpiperidin-4-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 135 N-[4-(N-[3-methylthio-1-carboxyprop-2-yl]aminocarbonyl)-2-phenylbenzoyl]-methionine,  
N-[4-N-(furan-2-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(furan-3-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 140 N-[4-N-benzyl-N-3-methoxyphenylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(2-phenylethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 145 N-[4-N-benzyl-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-N-(1,3-benzodiox-5-yl)-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(1,3-benzodiox-5-yl)-N-pyridizin-2-ylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 150 N-[4-(N-benzyl-N-(2-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 155 N-[4-(N-benzyl-N-(4-acetylphenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(N-benzyl-N-(3-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-nitrophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]-methionine, lithium salt,
- 160 N-[4-N-(N-benzyl-N-(2-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-benzyl-N-(3-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 165 N-[4-N-(N-benzyl-N-(2-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

- N-[4-N-(N-benzyl-N-(3-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 170 N-[4-N-(N-benzyl-N-(4-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-benzyl-N-(2-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
- N-[4-N-(N-benzyl-N-(2-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 175 N-[4-N-(N-benzyl-N-(3-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-benzyl-N-(4-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-benzyl-N-(4-trifluoromethylphenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 180 N-[4-N-(4-piperidin-1-ylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
- N-[4-N-(4-morpholin-1-ylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
- 185 N-[4-N-(4-phenoxyphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,
- N-[4-N-(benzyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,
- N-[4-N-(toluenesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- 190 N-[4-N-(methanesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(N-2-cyclohexylethyl-N-cyclopropylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
- 195 N-[4-N-(N-tetrahydrothiopyran-4-yl-N-thiazol-5-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-t-butyloxycarbonyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(3-cyclohexyl-1-oxo-1-piperidin-1-ylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 200 N-[4-N-(1-ethylthio-4-methylpentan-2-yl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,
- N-[4-N-(1-ethylthio-4-methylpentan-2-yl)-N-methylaminomethyl)-2-(2-

- 205 methylphenyl)benzoyl]methionine,  
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
210 N-[4-(N-acetyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-benzoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-benzenesulfoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
215 N-[4-(N-(N,N-dibutylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-(N-(N,N-dibutylacetamido)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(N,N-dibenzylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
220 N-[4-(N-(2-cyclohexylethyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-butanefulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
225 N-[4-(N,N-dibutylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-butanefulfonyl-N-(3-phenylpropyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
230 N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-2-(2-methylphenyl)benzoyl]methionine, hydrochloride,  
N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-2-(2-methylphenyl)benzoyl]methionine,  
235 N-[4-N-acetyl-N-(3-cyclohexyl-1-ethylthiopropyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-t-butyloxycarbonyl-N-(3-cyclohexyl-1-ethylthiopropyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
240 N-[4-N-benzoyl-N-(3-cyclohexyl-1-ethylthiopropyl)aminomethyl)-2-(2-

- 245 methylphenyl)-benzoyl]methionine,  
N-[4-N-butanefulfoyl-N-(3-cyclohexyl-1-ethylthiopropyl)amino-  
methyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-benzenesulfonyl-N-(3-cyclohexyl-1-ethylthiopropyl)amino-  
methyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-5-(4-chlorophenyl)furan-2-ylmethyl-N-isopropylaminomethyl)-  
2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-methyl-N-(1,1-dimethyl-2-phenylethyl)aminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
250 N-[4-(N-methyl-N-(1,1-dimethyl-2-cyclohexylethyl)aminomethyl)-2-(2-  
methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-2-cyclohexylethyl-N-thiazol-5-ylmethylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-(1-ethylthio-4-phenylbut-2-oxymethyl)-2-(2-methylphenyl)-benzoyl]-  
255 methionine,  
N-[4-N-benzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-benzyl-N-(4-carboxamidophenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
260 N-[4-N-benzyl-N-(4-sulfonamidophenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-N-benzoylsulfonamidophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-propionylphenyl)aminomethyl-2-(2-methylphenyl)-  
265 benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-benzoylphenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-(6-methylbenzthiazol-2-yl)phenyl)aminomethyl-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
270 N-[4-N-2,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-2,4-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-  
275 phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-vinylphenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,

- N-[4-N-3,5-difluorobenzyl-N-(4-acetylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 280 N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxyethyl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxy-1-phenylmethyl)phenyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 285 N-[4-N-3,5-difluorobenzyl-N-(4-(2-hydroxyethyl)phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-3,5-difluorobenzyl-N-(4-(2-tert-butyldimethylsiloxyethyl)phenyl)-aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-3,5-difluorobenzyl-N-(1-ethylthio-3-cyclohexylprop-2-yl)amino-methyl-2-(2-methylphenyl)benzoyl]methionine,
- 290 N-[4-(2-N-piperidin-1-ylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(2-N-2-methoxymethylpyrrolidin-1-ylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(4-trans-pentafluorophenoxycyclohexyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- 295 N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]glutamine, trifluoroacetic acid salt,
- N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]homocysteine, lithium salt,
- 300 N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]histidine, trifluoroacetic acid salt,
- N-[4-(N-cyclohexylmethylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N,N-di-(cyclohexylmethyl)aminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,
- 305 N-[4-(N-cyclohexylmethyl-N-phenylacetylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-(N-cyclohexylmethyl-N-1-adamantanoylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 310 N-[4-(N-cyclohexylmethyl-N-t-butoxycarbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-(N-cyclohexylmethyl-N-2-ethylhexyloxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-cyclohexylmethyl-N-2,2,2-trichloroethoxycarbonylaminoethyl)-2-(2-

- 315 methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-cyclohexyloxycarbonylaminoethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-adamantyloxycarbonylaminoethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
320 N-[4-(N-cyclohexylmethyl-N-phenoxy carbonylaminoethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-benzyloxycarbonylaminoethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminocarbonylaminoethyl)-2-(2-  
325 methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminothiocarbonylaminoethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]glutaminitrile, lithium salt,  
330 N-[4-(N-p-toluenesulfonyl-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-(4-benzyloxybenzyl)-N-(N-2-methyl-2-phenylpropylacetamido)-  
aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexenylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
335 benzoyl]methionine, lithium salt,  
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,  
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-  
methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,  
340 N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]norleucine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N,N-dimethylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine,  
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-  
345 benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-p-toluenesulfonylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-m-toluenesulfonylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
350 N-[4-(N-(2-cyclohexylethyl)-N-p-tert-butylbenzenesulfonylaminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,

- N-[4-(N-(2-cyclohexylethyl)-N-p-bromobenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 355 N-[4-(N-(2-cyclohexylethyl)-N-p-methoxybenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-(2-cyclohexylethyl)-N-p-nitrobenzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-(2-cyclohexyl-2-methylpropyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 360 N-[4-(3-cyclohexyl-1-methoxyprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- (2S)-2-N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,
- 365 N-[4-(N-(3-cyclohexylpropyl)-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-glucosaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 370 (2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-difluoromethylthiobutanoate, lithium salt,
- (2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-5-methoxypentanoate, lithium salt,
- (2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]aminopent-4-ynoate, lithium salt,
- 375 2-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]oxy-4-methylthiobutanoate, lithium salt,
- N-[4-(N-(5-bromo-(4-chlorophenyl)furan-2-yl)methyl-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 380 N-[4-(N-(5-phenyl-(4-chlorophenyl)furan-2-yl)methyl-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-(5-(3-methoxyphenyl)-(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-(4,5-di(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylamino-methyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 385 N-[4-(N-(5-thien-3-yl-(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methyl-

- phenyl)benzoyl]methionine, ...
- 390 N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
- 395 N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-2-N,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,
- 400 N-[4-(N-(1-benzyloxymethyl-2-(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]ornithine, trifluoroacetate salt,  
N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]thien-2-ylalanine,
- 405 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 410 N-[4-(N-butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylaminocarbonyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 415 N-[4-(N-cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 420 N-[4-(N-cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt,  
N-[4-(N-cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexyl-N-propanoylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine,
- 425 N-[4-(N-cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]-



- methionine, lithium salt,  
N-[4-(N-cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
430 methionine, lithium salt,  
N-[4-(N,N-dicyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-adamant-1-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
435 N-[4-(N-adamant-2-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-adamant-1-ylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-myrtanylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
440 methionine, lithium salt,  
N-[4-(N-cyclooctylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
lithium salt,  
3-[4-(N-cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-  
4-methylthiobutyric acid,  
445 N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,  
N-[4-(N-(2,2,4,4-tetramethylbutylamino)carbonylethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N,N-dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium  
450 salt,  
N-[4-N-(2-ethylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(4-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
455 N-[4-N-(2-butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-N-(2,6-diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(2-butylphenyl)-N-(cyclohexylmethyl)aminomethyl-2-(2-methylphenyl)-  
460 benzoyl]methionine, lithium salt,  
N-[4-N-(2-cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,

- N-[4-N-(2-butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- 465 N-[4-N-butyl-N-(2-(3,5-difluoro)phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-butanefulfonyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt,
- N-[4-N-(2-cyclohexylethyl)-N-methylaminomethyl-2-(2-methylphenyl)benzoyl]-3-aminotetrahydrofuran-2-one,
- 470 N-[4-N-(2-cyclohexylethyl)-N-butylaminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine 4-methylphenylsulfonimide,
- 475 N-[4-N-butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-t-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- 480 N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(2-cyclohexylethyl)-N-propyloxyaminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 485 N-[4-N-(2-cyclohexylethyl)-N-propanesulfonylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(3-chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(2-cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt,
- 490 N-[4-N-(2-cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 495 N-[4-N-(4-cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,
- N-[4-N-(butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-

- 500 methionine,  
N-[4-(N-butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-((1-norpholinocarbonyl)butyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
505 N-[4-N-butyl-N-(2-morpholin-4-ylethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine,  
N-[4-N-(2-cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl-2-(2-methyl-  
510 henyl)benzoyl]methionine,  
N-[4-N-butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-(2-butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,  
515 N-[4-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-  
520 methionine p-tolylsulfonimide, hydrochloride salt,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine 4-(aminomethyl)phenylsulfonimide, dihydrochloride salt,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, isopropylsulfonimide,  
525 N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(n-butanesulfonyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methyl-  
530 phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
535 N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,

- N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 540 N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 545 N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 550 N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- 555 N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
- 560 N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
- 565 N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 570 N-[4-N-(N-phenyl-N-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-

- benzoyl]methionine, lithium salt,
- 575 N-[4-N-(N-phenyl-N-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(2-methyl-4-methylemethiazolyl)aminomethyl)-2-  
(2-methylphenyl)benzoyl]methionine, lithium salt,
- 580 N-[4-N-(N-3,5-difluorophenyl-N-(5-thiazolylmethyl)aminomethyl)-2-  
(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(5-thiazolylmethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-  
(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,
- 585 N-[4-N-(N-(4-acetonitrilephenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-  
(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(4-nitrophenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-  
590 methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-butyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(4,4,4-trifluorobutyl-N-(3,5-difluorobenzyl)aminomethyl)-  
2-(2-methylphenyl)benzoyl]methionine, lithium salt,
- 595 N-[4-N-(N-cyclohexyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(4-cyclohexanonyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-  
(2-methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-N-(3,5-  
600 difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium  
salt,
- N-[4-N-(N-cyclohexylmethyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-cyclohexylmethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-  
605 methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(4-cyanobenzyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,
- N-[4-N-(N-(3,5-difluorobenzyl)-N-(4-N-carboxymethionine)benzyl)-  
aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,
- 610 N-[4-N-(N-(2-cyclohexylethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-

- (2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-  
 2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-cyclopropyl-N-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-  
 2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 [4-N-(N-2-methylbutyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-  
 (2-methylphenyl)benzoyl]methionine, lithium salt,  
 [4-N-(N-butyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-  
 methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-(4-methyltetrahydropyran-yl)-N-(3,5-difluorobenzyl)-  
 aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-(4-methyltetrahydrothiopyran-yl)-N-(3,5-difluorobenzyl)-  
 aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-  
 methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-(N-(3-cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-  
 methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,  
 N-[4-(N-methyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-  
 methylphenyl)benzoyl]methionine, p-tolylsulfonimide,  
 N-[4-N-(N-(trans-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-  
 2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-(cis-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-  
 (2-methylphenyl)benzoyl]methionine, lithium salt,  
 (2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-  
 methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,  
 N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-  
 benzoyl]methionine,  
 N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
 benzoyl]thioglutamine, lithium salt,  
 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-  
 methylphenyl)benzoyl]methionine,  
 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N,N'-dimethyl-  
 amino-2-(2-methylphenyl)benzoyl]methionine,  
 N-[4-N-(6-fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)-  
 benzoyl]methionine, and  
 N-[4-N-butyl-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
 methionine.

10. A compound selected from the group consisting of
- [4-(thiazo-4-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - [4-(thiazol-2-ylmethylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - [4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine, methyl ester, hydrochloride,
  - [4-((R)-thiazolidin-4-ylcarbonyl)amino-2-phenylbenzoyl]methionine,
  - [4-((R)-thiazolidin-4-ylmethyl)amino-2-phenylbenzoyl]methionine, hydrochloride,
  - [4-(4-hydroxy-prolinyl)amino-2-phenylbenzoyl]methionine, trifluoroacetate,
  - [4-((2S,4S)-4-mercaptopyrrolidin-2-carboxy)amino-2-phenylbenzoyl]-methionine, trifluoroacetate,
  - [4-((2S,4R)-4-hydroxypyrrolidin-2-ylmethyl)amino-2-phenylbenzoyl]-methionine, hydrochloride,
  - [4-((2S,4S)-4-thiopyrrolidin-2-yl-methylamino)-2-phenylbenzoyl]-methionine, hydrochloride,
  - [4-(1H-benzimidazol-5-ylcarboxyamino)-2-phenylbenzoyl]methionine, trifluoroacetate,
  - [4-(piperidin-2-ylcarboxyamino)-2-phenylbenzoyl]methionine, hydrochloride,
  - [4-(2-pyrrolidinone-5-ylcarbonylamino)-2-phenylbenzoyl]methionine,
  - [4-(5-pyrimidylcarboxyamino)-2-phenylbenzoyl]methionine,
  - [4-(3-piperidinecarboxyamino)-2-phenylbenzoyl]methionine, hydrochloride,
  - [4-(1H-4-trifluoromethyl-1,2-dihydropyrid-3-ylcarbonylamino)-2-phenylbenzoyl]methionine, sodium salt,
  - [4-(2-piperazinylmethylamino)-2-phenylbenzoyl]methionine,
  - [4-(2-furylmethylaminomethyl)-2-phenylbenzoyl]methionine lithium salt,
  - N-[4-N-2-hydroxyethylamino-2-phenylbenzoyl]methionine,
  - N-[4-(N-2-amino-3-benzyloxypropionyl)amino-2-phenylbenzoyl]methionine,
  - N-[4-N-phenyl-N-benzylaminomethyl-2-phenylbenzoyl]methionine,
  - N-[4-N-(2-hydroxyethyl)-N-benzylaminomethyl-2-phenylbenzoyl]methionine, lithium salt,
  - N-[4-N-(t-butylcarbazonocarbonylmethyl)amino-2-phenylbenzoyl]methionine,
  - N-[4-N,N-dibenzylaminomethyl-2-phenylbenzoyl]methionine, lithium salt,
  - N-[4-N-(benzyl-N-thiazol-5-ylmethyl)aminomethyl-2-phenylbenzoyl]-methionine,

N-[4-(N-benzylaminomethyl)-2-phenylbenzoyl]methionine, hydrochloride salt,  
N-[4-(4-hydroxyprolinylamino)-2-phenylbenzoyl]methionine,  
N-[4-((2S,4S)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine,  
N-[4-((2S,4R)-4-thiolpyrrolidin-2-ylmethylamino)-2-phenylbenzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-phenylbenzoyl]-  
methionine, lithium salt,  
[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine,  
4-(N-benzyl-N-phenyl)-aminomethyl-2-(2-methylphenyl)benzoylmethionine,  
N-[4-N-(2,2-dibenzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-  
methionine, sodium salt,  
N-[4-N-(2-benzyl-3-hydroxypropyl)amino-2-(2-methylphenyl)benzoyl]-  
methionine, sodium salt,  
N-[4-N-(2-cyclohexylmethyl-3-hydroxypropyl)amino-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-(furan-2-ylmethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-(2-benzylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-phenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine,  
N-[4-N-(3-phenyl)propyl-N-phenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine,  
N-[4-N-(2,2-diphenyl)ethyl-N-phenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-(adamantan-1-ylmethyl)-N-phenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-(2-adamantan-1-ylethyl)-N-phenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N,N-dibenzylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,  
N-[4-N-(2-phenylethyl)-N-benzylaminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-(3-phenoxybenzyl)-N-benzylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-methyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-benzyl-N-pyrazin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-



methionine, lithium salt,  
N-[4-N-(2-phenylethyl)-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(2-indol-3-ylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-N-(2-cyclohexyl-1-ethan-1-ol-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(1,3-diphenylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(1-cyclohexyl-6-methylhept-3-en-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(1-cyclohexyl-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(1-cyclohexyl-2,3-dihydroxy-6-methylheptan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(3-furan-2-yl-2-phenylprop-2-en-1-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, methyl ester,  
N-[4-N-phenylacetyl-amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(4'-methylphenylacetyl)amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(4'-methoxyphenylacetyl)amino-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-N-(3-phenylpropionoyl)amino-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(3-(2-methoxyphenyl)propionoyl)amino-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-N-benzyl-N-(thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-benzyl-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,

N-[4-(2-cyclohexylethan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(N-benzyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-2-cyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, trifluoroacetate salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-acetyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-(N,N-dimethylaminocarbonyl)-N-(2-cyclohexylethyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-methanesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-benzenesulfonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine lithium salt,  
N-[4-(3-cyclohexylpropan-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-(4-cyclohexylbutan-3-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(6-cyclohexylhexan-5-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(1,2-dicyclohexylethylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-(3-cyclohexylpropan-1-ol-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, trifluoroacetate salt,  
N-[4-(2-cyclohexylprop-1-en-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(3-cyclohexyl-1-ethylsulfonylpropan-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(3-cyclohexyl-1-ethylsulfonylpropan-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]-2-amino-4-methanesulfonylbutanoic acid, lithium salt,  
N-[4-(3-cyclohexyl-1-t-butylthioprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(3-cyclohexyl-1-phenylthioprop-2-ylaminomethyl)-2-(2-methylphenyl)-

benzoyl]methionine, lithium salt,  
N-[4-N-benzoyl-N-2-cyclohexylethylaminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-t-butyloxycarbonyl-N-2-cyclohexylethylaminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
pivaloyloxymethyl N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-N-methyl-  
aminomethyl-2-(2-methylphenyl)benzoyl]methionine, hydrochloride salt,  
N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-N-methylaminomethyl-2-  
(2-methylphenyl)benzoyl]-N-methylmethionine, lithium salt,  
N-[4-N-(3-cyclohexyl-1-cyclohexylthiopropyl)-N-methylamino-  
methyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(3-cyclohexyl-1-(2-methylphenyl)thiopropyl)-N-methyl-  
aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-toluenesulfonylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(3-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzenesulfonyl)aminomethyl)-  
2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-chlorobenzyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-trifluoromethylbenzyl)aminomethyl)-2-(2-  
methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(t-butylcarbazatocarbonylmethyl)amino-2-phenylbenzoyl]methionine,  
N-[4-(1-ethoxycarbonylpiperidin-4-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-[3-methylthio-1-carboxyprop-2-yl]aminocarbonyl)-2-phenylbenzoyl]-  
methionine,  
N-[4-N-(furan-2-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(furan-3-ylmethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-3-methoxyphenylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(2-phenylethyl)-N-isopropylaminomethyl-2-(2-methylphenyl)-

benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-pyrimidin-5-ylaminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-(1,3-benzodiox-5-yl)-N-pyrimidin-5-ylaminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(1,3-benzodiox-5-yl)-N-pyridizin-2-ylaminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(2-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-methoxyphenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-acetylphenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-benzyl-N-(3-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-nitrophenyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]-  
methionine, lithium salt,  
N-[4-N-(N-benzyl-N-(2-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-benzyl-N-(3-acetylphenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-benzyl-N-(2-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-benzyl-N-(3-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(N-benzyl-N-(4-chlorophenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(2-nitrophenyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-benzyl-N-(2-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(3-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-methylthiophenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-benzyl-N-(4-trifluoromethylphenyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,

N-[4-N-(4-piperidin-1-yl)phenyl]aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-N-(4-morpholin-1-yl)phenyl]aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-N-(4-phenoxyphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-N-(benzyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(toluenesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(methanesulfonyl-N-thiazol-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-2-cyclohexylethyl-N-cyclopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-tetrahydrothiopyran-4-yl-N-thiazol-5-ylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-t-butyloxycarbonyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(3-cyclohexyl-1-oxo-1-piperidin-1-ylpropan-2-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(1-ethylthio-4-methylpentan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(1-ethylthio-4-methylpentan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(1,3-dicyclohexylpropan-2-yl)-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-acetyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-benzoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-benzenesulfoyl-N-(1,3-dicyclohexylpropan-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(N,N-dibutylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-(N-(N,N-dibutylacetamido)-N-methylaminomethyl)-2-(2-methylphenyl)-

benzoyl]methionine,  
N-[4-(N-(N,N-dibenzylacetamido)aminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-(N-butanefonyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-(N,N-dibutylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-butanefonyl-N-(3-phenylpropyl)aminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine,  
N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-N-methylaminomethyl-2-  
(2-methylphenyl)benzoyl]methionine, hydrochloride,  
N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-N-isobutylaminomethyl-  
2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(3-cyclohexyl-1-ethylthiopropyl)-N-formylaminomethyl-2-  
(2-methylphenyl)benzoyl]methionine,  
N-[4-N-acetyl-N-(3-cyclohexyl-1-ethylthiopropyl)aminomethyl-2-(2-  
methylphenyl)benzoyl]methionine,  
N-[4-N-t-butyloxycarbonyl-N-(3-cyclohexyl-1-ethylthiopropyl)amino-  
methyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-benzoyl-N-(3-cyclohexyl-1-ethylthiopropyl)aminomethyl-2-(2-  
methylphenyl)-benzoyl]methionine,  
N-[4-N-butanefonyl-N-(3-cyclohexyl-1-ethylthiopropyl)amino-  
methyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-benzenesulfonyl-N-(3-cyclohexyl-1-ethylthiopropyl)amino-  
methyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-5-(4-chlorophenyl)furan-2-ylmethyl-N-isopropylaminomethyl)-  
2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-methyl-N-(1,1-dimethyl-2-phenylethyl)aminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-methyl-N-(1,1-dimethyl-2-cyclohexylethyl)aminomethyl)-2-(2-  
methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-2-cyclohexylethyl-N-thiazol-5-ylmethylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-(1-ethylthio-4-phenylbut-2-oxymethyl)-2-(2-methylphenyl)-benzoyl]-

methionine,  
N-[4-N-benzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-N-benzyl-N-(4-carboxamidophenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-sulfonamidophenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-N-benzoylsulfonamidophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-propionylphenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-benzoylphenyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-benzyl-N-(4-(6-methylbenzthiazol-2-yl)phenyl)aminomethyl-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-2,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-2,4-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-cyanophenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-vinylphenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-acetylphenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxyethyl)phenyl)aminomethyl-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-(1-hydroxy-1-phenylmethyl)phenyl)-  
aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-(2-hydroxyethyl)phenyl)aminomethyl-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(4-(2-tert-butyldimethylsiloxyethyl)phenyl)-  
aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-3,5-difluorobenzyl-N-(1-ethylthio-3-cyclohexylprop-2-yl)amino-  
methyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(2-N-piperidin-1-ylaminoethenyl)-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,

N-[4-(2-N-2-methoxymethylpyrrolidin-1-ylaminoethenyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(4-trans-pentafluorophenoxy)cyclohexyl]aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]glutamine, trifluoroacetic acid salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]homocysteine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]histidine, trifluoroacetic acid salt,  
N-[4-(N-cyclohexylmethylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N,N-di-(cyclohexylmethyl)aminoethyl)-2-(2-methylphenyl)benzoyl]-methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-phenylacetylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-1-adamantanoylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-t-butoxycarbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-2-ethylhexyloxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-2,2,2-trichloroethoxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-cyclohexyloxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-adamantyloxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-phenoxy carbonylaminoethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-benzyloxycarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminocarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-adamant-1-aminothiocarbonylaminoethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-



benzoyl]glutaminitrile, lithium salt,  
N-[4-(N-p-toluenesulfonyl-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-(4-benzyloxybenzyl)-N-(N-2-methyl-2-phenylpropylacetamido)-  
aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,  
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-  
methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]norleucine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N,N-dimethylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine,  
(2S) 2-N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-p-toluenesulfonylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-m-toluenesulfonylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-p-tert-butylbenzenesulfonylaminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-p-bromobenzenesulfonylaminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-p-methoxybenzenesulfonylaminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-p-nitrobenzenesulfonylaminomethyl)-2-(2-  
methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexyl-2-methylpropyl)-N-methylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-(3-cyclohexyl-1-methoxyprop-2-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
(2S) 2-N-[4-(1-ethylsulfenyl-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methyl-  
phenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,

N-[4-(N-(3-cyclohexylethyl)-N-benzenesulfonylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-glucosaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-difluoromethylthiobutanoate, lithium salt,  
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-5-methoxypentanoate, lithium salt,  
(2S)-2-N-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]aminopent-4-ynoate, lithium salt,  
2-[4-(N-2-cyclohexylethyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoyl]oxy-4-methylthiobutanoate, lithium salt,  
N-[4-(N-(5-bromo-(4-chlorophenyl)furan-2-yl)methyl-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(5-phenyl-(4-chlorophenyl)furan-2-yl)methyl-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(5-(3-methoxyphenyl)-(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(4,5-di(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(5-thien-3-yl-(4-chlorophenyl)furan-2-yl)methyl)-N-isopropylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-2-fluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-2,2,2-trifluoroethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-(2-cyclohexylethyl)-N-2-methoxyethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-2-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-1-methyl-2(S)-methylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-2,N-dimethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(1-benzyloxymethyl-2-(S)-ethylthioethylaminomethyl)-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-

benzoyl]ornithine, trifluoroacetate salt,  
N-[4-(N-(2-cyclohexylethyl)-N-2-N-methylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]thien-2-ylalanine,  
N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-fluoro-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-(N-butyl-N-4-cyclohexylbenzylaminomethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-butyl-N-4-cyclohexylbenzoylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-butylaminocarbonylmethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexanoyl-N-butylaminoethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-cyclohexylmethyl-N-butanoylaminoethyl)-2-(2-methylphenyl)benzoyl]-  
methionine lithium salt,  
N-[4-(N-cyclohexylpropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-(N-cyclohexyl-N-propanoylaminoethyl)-2-(2-methylphenyl)benzoyl]-  
methionine,  
N-[4-(N-cyclohexyl-N-butylaminopropyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-cyclohexyl-N-methylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-cyclohexyl-N-butylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N,N-dicyclohexylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-adamant-1-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-adamant-2-ylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-adamant-1-ylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-  
methionine, lithium salt,  
N-[4-(N-mytanylmethylaminocarbonylethyl)-2-(2-methylphenyl)benzoyl]-

methionine, lithium salt,  
N-[4-(N-cyclooctanylaminocarbonyl)ethyl]-2-(2-methylphenyl)-benzoyl]-methionine,  
lithium salt,  
3-[4-(N-cyclohexyl-N-methylaminomethyl)-2-(2-methylphenyl)benzoylmethyl]-  
4-methylthiobutyric acid,  
N-[4-(N-butylaminocarbonylmethyl)-2-(2-methylphenyl)benzoyl]methionine,  
lithium salt,  
N-[4-(N-(2,2,4,4-tetramethylbutylamino)carbonyl)ethyl]-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-(N,N-dibutylaminopropyl)-2-(2-methylphenyl)benzoyl]methionine, lithium  
salt,  
N-[4-N-(2-ethylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-propylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(4-butylphenyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-butylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-N-(2,6-diethylphenyl)-N-(3,5-difluorobenzyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(2-butylphenyl)-N-(cyclohexylmethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-(2-cyclohexylethyl)-N-(3-methylphenyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-N-(2-butylphenyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methyl-  
phenyl)benzoyl]methionine,  
N-[4-N-butyl-N-(2-(3,5-difluoro)phenylethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,  
N-[4-N-butanefonyl-N-(2-phenylethyl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine lithium salt,  
N-[4-N-(2-cyclohexylethyl)-N-methylaminomethyl-2-(2-methylphenyl)-  
benzoyl]-3-aminotetrahydrofuran-2-one,  
N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-  
benzoyl]methionine, lithium salt,  
N-[4-N-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-  
methionine 4-methylphenylsulfonimide,  
N-[4-N-butyl-N-(1-phenyltetrazol-5-yl)aminomethyl-2-(2-methylphenyl)-  
benzoyl]methionine,

N-[4-N-t-butyl-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-(2-cyclohexylethyl)-N-(pent-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-(2-cyclohexylethyl)-N-propyloxyaminomethyl-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(2-cyclohexylethyl)-N-propanesulfonylaminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(3-chloropropanesulfonyl)-N-(2-cyclohexylethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(2-cyclohexylethyl)-N-(3-ethoxypropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine lithium salt,  
N-[4-N-(2-cyclohexylethyl)-N-(3-trifluoromethylpropanesulfonyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-(butanesulfonyl)-N-(3-cyclohexylpropyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(4-cyclohexyl-1-ethylthiobutan-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-(butanesulfonyl)-N-(4-cyclohexylbutyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-butyl-N-quinolin-2-ylaminomethyl-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-(N-butyl-N-(2-piperidin-1-ylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-((1-norpholinocarbonyl)butyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-butyl-N-(2-morpholin-4-ylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-butyl-N-(fluoren-9-yl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine,  
N-[4-N-(2-cyclohexylethyl)-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-N-butyl-N-(2-pyrrolidin-1-ylethyl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-(2-butylphenyl)-N-(thiazol-5-ylmethyl)aminomethyl-2-(2-methyl-

phenyl)benzoyl]methionine,  
N-[4-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine,  
N-[4-N-butyl-N-((2-ethylthio)-1,3,4-thiadiazol-5-yl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]-methionine p-tolylsulfonimide, hydrochloride salt,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine 4-(aminomethyl)phenylsulfonimide, dihydrochloride salt,  
N-[4-(N-butyl-N-(2-phenylethyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, isopropylsulfonimide,  
N-[4-N-(N-phenyl-N-(4-fluorobenzoyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(n-butanefonyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(3-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-fluorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-ethylbenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-nitrobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2,3-dichlorobenzenesulfonyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-3,4-(methylenedioxy)phenyl-N-(4-fluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(3-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-fluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-bromobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,

N-[4-N-(N-phenyl-N-(4-cyanobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-trifluoromethoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-nitrobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-carboxylic acid benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,  
N-[4-N-(N-phenyl-N-(4-phenylbenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(4-N-carboxymethionine)benzyl)aminomethyl-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,  
N-[4-N-(N-phenyl-N-(2-naphthyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(9-methyl-anthracene-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2-methyl-anthraquinone-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2,3-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2-thiophenesulfonyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(2-methyl-4-methylemethiazolyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-3,5-difluorophenyl-N-(5-thiazolylmethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(5-thiazolylmethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-acetonitrilephenyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-phenyl-N-(3-methoxy-5-nitrobenzyl)aminomethyl)-2-(2-

methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-nitrophenyl)-N-(4-methoxybenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-butyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4,4,4-trifluorobutyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-cyclohexyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-cyclohexanonyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-(2,2-dimethyltrimethylene ketal)-cyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-cyclohexylmethyl-N-(2,4-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-cyclohexylmethyl-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-cyanobenzyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(3,5-difluorobenzyl)-N-(4-N-carboxymethionine)benzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, dilithium salt,  
N-[4-N-(N-(2-cyclohexylethyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(3-methylthiopropyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-cyclopropyl-N-(2-(3,5-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
[4-N-(N-2-methylbutyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
[4-N-(N-butyl-N-(2-(2,4-difluorophenyl)ethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-methyltetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-methyltetrahydrothiopyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
N-[4-N-(N-(4-tetrahydropyran-yl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-



methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-(N-(3-cyclohexyl-1-ethylthioprop-2-yl)aminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfonylbutanoate, lithium salt,  
 N-[4-(N-methyl-N-(2-cyclohexylethyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, p-tolylsulfonimide,  
 N-[4-N-(N-(trans-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 N-[4-N-(N-(cis-4-hydroxycyclohexyl)-N-(3,5-difluorobenzyl)-aminomethyl)-2-(2-methylphenyl)benzoyl]methionine, lithium salt,  
 (2S) 2-N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)benzoyl]amino-4-methylsulfenylbutanoate, lithium salt,  
 N-[4-(N-(2-(1,3-dioxan-2-ylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine,  
 N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]thioglutamine, lithium salt,  
 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-methoxy-2-(2-methylphenyl)benzoyl]methionine,  
 N-[4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-5-N'-dimethyl-amino-2-(2-methylphenyl)benzoyl]methionine,  
 N-[4-N-(6-fluorobenzothiazol-2-yl)aminomethyl-2-(2-methylphenyl)-benzoyl]methionine, and  
 N-[4-N-butyl-N-(furan-2-ylmethyl)aminomethyl-2-(2-methylphenyl)benzoyl]-methionine.

11. A compound according to claim 10 selected from the group consisting of [4-(1-ethylthio-3-cyclohexylprop-2-ylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, N-[4-(N-(2-cyclohexylethyl)-N-methylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt, and N-[4-(N-(2-cyclohexylethyl)-N-butylaminomethyl)-2-(2-methylphenyl)-benzoyl]methionine, lithium salt.
12. A method of inhibiting protein isoprenyl transferases in a mammal in need of such treatment comprising administering to the mammal a therapeutically effective amount of a compound of claim 1.
13. A composition for inhibiting protein isoprenyl transferases comprising a

pharmaceutical carrier and a therapeutically effective amount of a compound of claim 1.

14. A method for inhibiting or treating cancer in a mammal, comprising administering to the mammal a therapeutically effective amount of a compound of claim 1 alone or in combination with another chemotherapeutic agent.
15. A composition for the treatment of cancer comprising a compound of claim 1 in combination with another chemotherapeutic agent and a pharmaceutically acceptable carrier.
16. A method for inhibiting post-translational modification of the oncogenic Ras protein by protein farnesyltransferase, protein geranylgeranyltransferase, or both in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of claim 1.
- 5 17. A composition for inhibiting post-translational modification of the oncogenic Ras protein by protein farnesyltransferase, protein geranylgeranyltransferase, or both comprising a compound of claim 1 in combination with a pharmaceutical carrier.
- 5 18. A method for treating or preventing intimal hyperplasia associated with restenosis and atherosclerosis in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of claim 1.
19. A composition for treating or preventing restenosis in a mammal comprising a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/09296

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database HCAPLUS on STN, 1997:247953, BOYLE, F.T. et al. 'Preparation of 2-aminomethyl-4-mercaptopyrrolidines and analogs as farnesyl transferase inhibitors', 20 February 1997, PCT Int. Appl. 189 pp., see the entire abstract.	1-19
X	Database HCAPLUS on STN. 1996:567259 SEBTI et al. 'Peptidomimetic inhibitors of prenyl transferase, preparation and activity of the peptidomimetics, and use for treating tumors', 18 July 1996, PCT Int. Appl 186 pp., see the entire abstract.	1-19

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

07 SEPTEMBER 1998

Date of mailing of the international search report

16 OCT 1998

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/09296

## A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

A61K 31/38, 31/39, 31/40, 31/415, 31/42, 31/425, 31/44, 31/445, 31/495, 31/505, 31/095, 31/18; C07D 207/09, 233/54, 239/24, 241/04, 263/02, 277/28, 307/00, 333/00, 209/10;  
C07C 303/00, 307/00, 309/00, 311/00, 313/00

## A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

514/255, 256, 331, 351, 357, 371, 400, 419, 423, 424, 439, 447, 461, 570, 604; 544/335, 400 ; 546/225, 300, 312, 336;  
548/196, 338.1, 495, 543; 549/69, 76, 491; 564/42, 49

## B. FIELDS SEARCHED

Minimum documentation searched

Classification System: U.S.

514/255, 256, 331, 351, 357, 371, 400, 419, 423, 424, 439, 447, 461, 570, 604; 544/335, 400 ; 546/225, 300, 312, 336;  
548/196, 338.1, 495, 543; 549/69, 76, 491; 564/42, 49